بسم الله الرحمن الرحيم

Heart Failure 4th year

Heart failure

Heart failure describes the clinical syndrome that develops when the heart cannot maintain adequate output, or can do so only at the expense of elevated ventricular filling pressure.

In mild to moderate forms of heart failure, cardiac output is normal at rest and only becomes impaired when the metabolic demand increases during exercise or some other form of stress.

In practice, heart failure may be diagnosed when a patient with significant heart disease develops the signs or symptoms of a low cardiac output, pulmonary congestion or systemic venous congestion.

Heart Failure

Definition

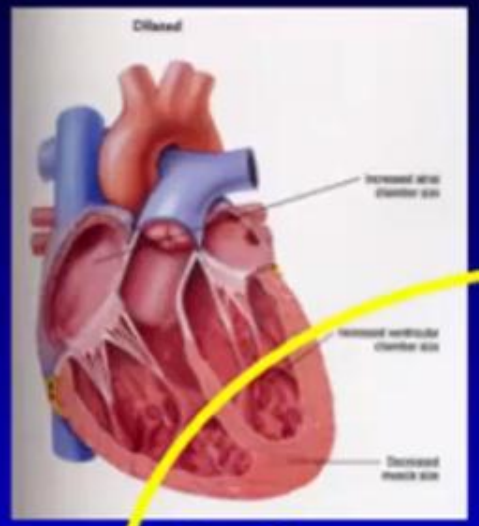
- It is the pathophysiological process in which the heart as a pump is unable to meet the metabolic requirements of the tissue for oxygen and substrates despite the venous return to heart is either normal or increased

DEFINITION (ACC 2013)

A complex clinical syndrome that results from any structural or functional impairment of ventricular filling or ejection of blood.

It may result from disorders of the pericardium, myocardium , endocardium, heart valves, great vessels or from certain metabolic abnormaities (but most patients with HF have symptoms due to impaired LV myocardial function).

The syndrome of Chronic Heart Failure



Dyspnoea
Fatigue

Left
Ventricular
Dysfunction

CHF

Congestion
Lungs
Limbs
Guts

Preload and Afterload

Preload: volume entering ventricles

Afterload: resistance left ventricle must overcome to circulate blood

Factors Effecting Heart Pump Effectiveness

Preload

- Volume of blood in ventricles at end diastole
- Depends on venous return
- Depends on compliance

Afterload

- Force needed to eject blood into circulation
- Depends upon arterial BP, pulmonary artery pressure
- Valvular disease increases afterload

Ejection Fraction (EF)

- One of the measurements used by physicians to assess how well a patient's heart is functioning
- "Ejection" refers to the amount of blood that is pumped out of the heart's main pumping chamber during each heartbeat
- "Fraction" refers to the fact that, even in a healthy heart, some blood always remains within this chamber after each heartbeat
- An ejection fraction is a percentage of the blood within the chamber that is pumped out with every heartbeat
- Normal EF = 55 to 75 percent

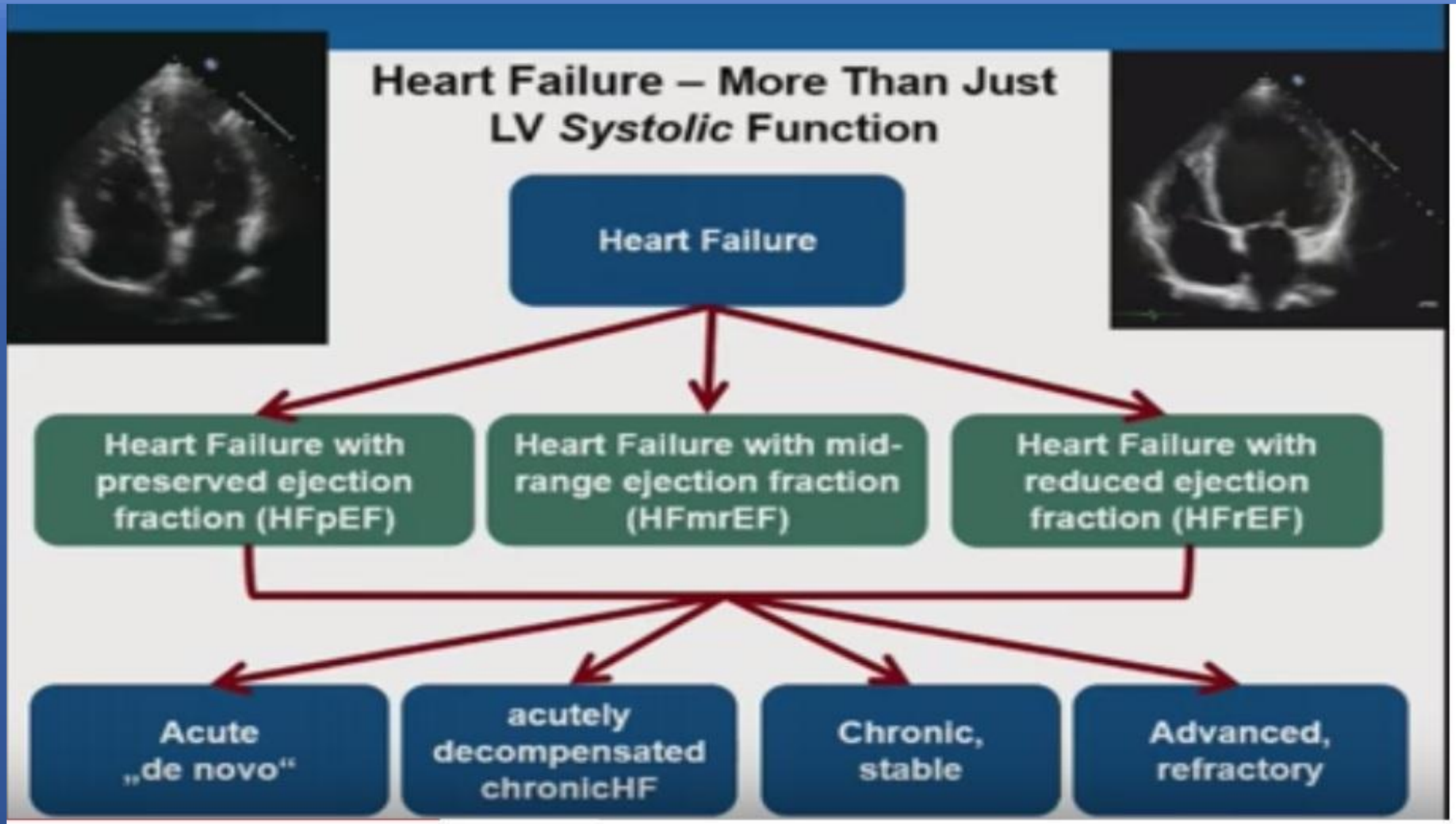

Heart Failure – More Than Just LV *Systolic* Function
Heart Failure
Heart Failure with preserved ejection fraction (HFpEF)
Heart Failure with mid-range ejection fraction (HFmrEF)
Heart Failure with reduced ejection fraction (HFrEF)
Acute „de novo“
acutely decompensated chronicHF
Chronic, stable
Advanced, refractory

Table 1. Definitions of HF*r*EF and HF*p*EF

Classification	EF	Description
I. Heart failure with reduced ejection fraction (HF*r*EF)	≤40%	Also referred to as "systolic HF." Randomized clinical trials have mainly enrolled patients with HF*r*EF, and it is only in these patients that efficacious therapies have been demonstrated to date.
II. Heart failure with preserved ejection fraction (HF*p*EF)	≥50%	Also referred to as "diastolic HF." Several different criteria have been used to further define HF*p*EF. The diagnosis of HF*p*EF is challenging because it is largely one of excluding other potential noncardiac causes of symptoms suggestive of HF. To date, efficacious therapies have not been identified.
IIa. HF*p*EF, borderline	41%–49%	These patients fall into a borderline or intermediate group. Their characteristics, treatment patterns, and outcomes appear similar to those of patients with HF*p*EF.
IIb. HF*p*EF, improved	>40%	It has been recognized that a subset of patients with HF*p*EF previously had HF*r*EF. These patients with improvement or recovery in EF may be clinically distinct from those with persistently preserved or reduced EF. Further research is needed to better characterize these patients.

18.11 Mechanisms of heart failure

Cause	Examples	Features
Reduced ventricular contractility	MI (segmental dysfunction)	In coronary artery disease, 'akinetic' or 'dyskinetic' segments contract poorly and may impede the function of normal segments by distorting their contraction and relaxation patterns
	Myocarditis/cardiomyopathy (global dysfunction)	Progressive ventricular dilatation
Ventricular outflow obstruction (pressure overload)	Hypertension, aortic stenosis (left heart failure) Pulmonary hypertension, pulmonary valve stenosis (right heart failure)	Initially, concentric ventricular hypertrophy allows the ventricle to maintain a normal output by generating a high systolic pressure. Later, secondary changes in the myocardium and increasing obstruction lead to failure with ventricular dilatation and rapid clinical deterioration
Ventricular inflow obstruction	Mitral stenosis, tricuspid stenosis	Small, vigorous ventricle, dilated hypertrophied atrium. Atrial fibrillation is common and often causes marked deterioration because ventricular filling depends heavily on atrial contraction
Ventricular volume overload	Ventricular septal defect Right ventricular volume overload (e.g. atrial septal defect) Increased metabolic demand (high output)	Dilatation and hypertrophy allow the ventricle to generate a high stroke volume and help to maintain a normal cardiac output. However, secondary changes in the myocardium lead to impaired contractility and worsening heart failure
Arrhythmia	Atrial fibrillation	Tachycardia does not allow for adequate filling of the heart, resulting in reduced cardiac output and back pressure
	Tachycardia cardiomyopathy	Incessant tachycardia causes myocardial fatigue
	Complete heart block	Bradycardia limits cardiac output, even if stroke volume is normal
Diastolic dysfunction	Constrictive pericarditis	Marked fluid retention and peripheral oedema, ascites, pleural effusions and elevated jugular veins
	Restrictive cardiomyopathy	Bi-atrial enlargement (restrictive filling pattern and high atrial pressures). Atrial fibrillation may cause deterioration
	Left ventricular hypertrophy and fibrosis	Good systolic function but poor diastolic filling
	Cardiac tamponade	Hypotension, elevated jugular veins, pulsus paradoxus, poor urine output

Although the outlook depends, to some extent, on the underlying cause of the problem, untreated heart failure carries a poor prognosis; approximately 50% of patients with severe heart failure due to left ventricular dysfunction will die within 2 years, because of either pump failure or malignant ventricular arrhythmias.

Heart Failure
Etiology

- *Systolic Failure* - ***most common***
  - Hallmark finding: Decrease in ***left ventricular ejection fraction <40%*** (EF)
    - Due to
      - Impaired contractile function (e.g., MI)
      - Increased afterload (e.g., hypertension)
      - Cardiomyopathy
      - Mechanical abnormalities (e.g., valve disease)

Heart Failure
Etiology

Diastolic failure

- Impaired ability of ventricles to relax and fill during diastole ➔ decrease stroke volume and CO
- Diagnosis based on presence of pulmonary congestion, pulmonary hypertension, ventricular hypertrophy
- **Normal ejection fraction (EF)-** ***Know why!***

Not have much blood to eject

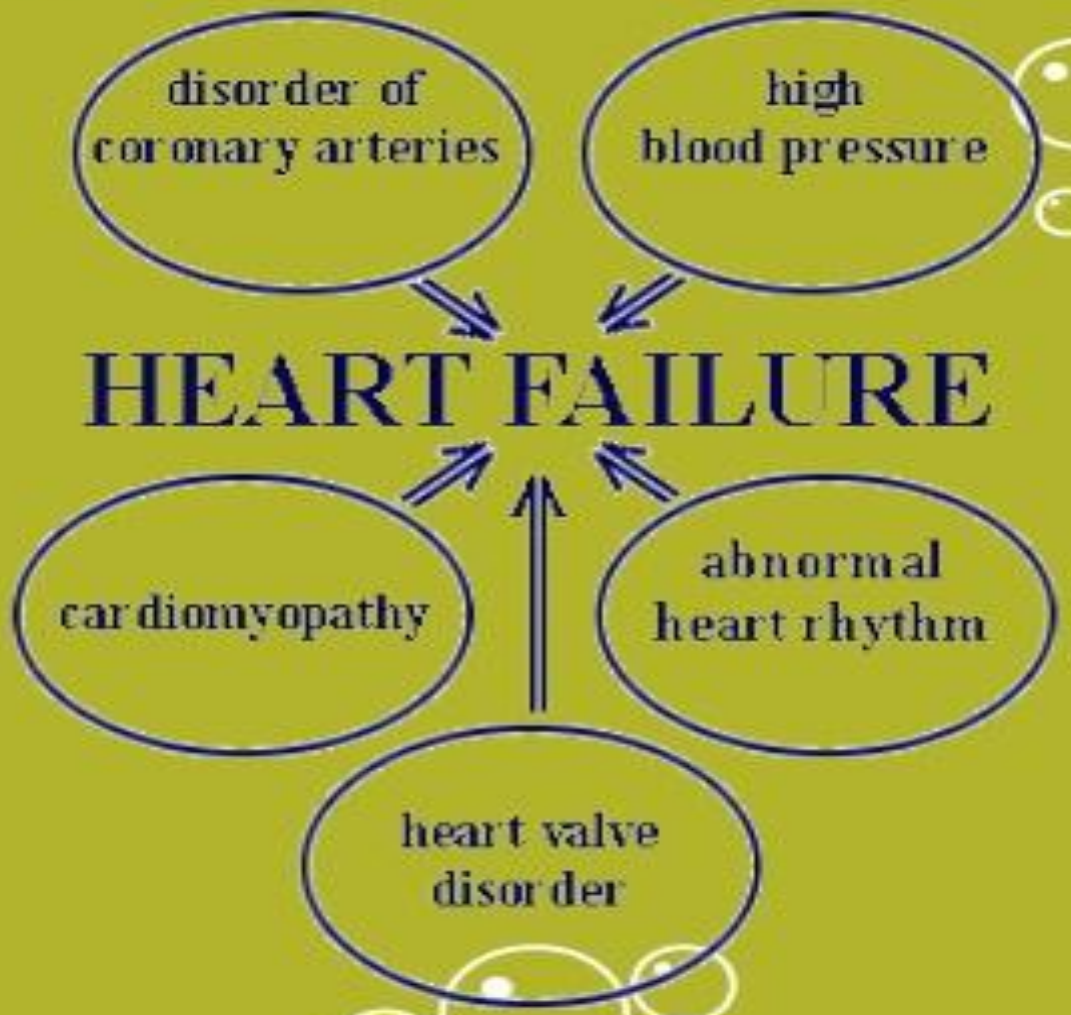
Heart Failure
Etiology

- ***Mixed systolic and diastolic failure***
  - Seen in disease states such as dilated cardiomyopathy (DCM)
  - Poor EFs (<35%)
  - High pulmonary pressures

- ***Biventricular failure***
  - Both ventricles may be dilated and have poor filling and emptying capacity

Heart Failure
Risk Factors

- ***Primary risk factors***
  - Coronary artery disease (CAD)
  - Advancing age
- ***Contributing risk factors***
  - Hypertension
  - Diabetes
  - Tobacco use
  - Obesity
  - High serum cholesterol
  - African American descent
  - Valvular heart disease
  - Hypervolemia



Heart Failure

Causes

1. ***Impaired cardiac function***
   - Coronary heart disease
   - Cardiomyopathies
   - Rheumatic fever
   - Endocarditis
1. ***Increased cardiac workload***
   - Hypertension
   - Valvular disorders
   - Anemias
   - Congenital heart defects
1. ***Acute non-cardiac conditions***
   - Volume overload
   - Hyperthyroid, Fever,infection

Pathophysiology

Cardiac output is determined by preload (the volume and pressure of blood in the ventricles at the end of diastole), afterload (the volume and pressure of blood in the ventricles during systole) and myocardial contractility; this is the basis of Starling's Law

In patients without valvular disease, the primary abnormality is impairment of ventricular myocardial function, leading to a fall in cardiac output. This can occur because of impaired systolic contraction, impaired diastolic relaxation, or both.

Stimulation of the renin–angiotensin–aldosterone system leads to vasoconstriction, sodium and water retention, and sympathetic nervous system activation.

This is mediated by angiotensin II, a potent constrictor of arterioles, in both the kidney and the systemic circulation .

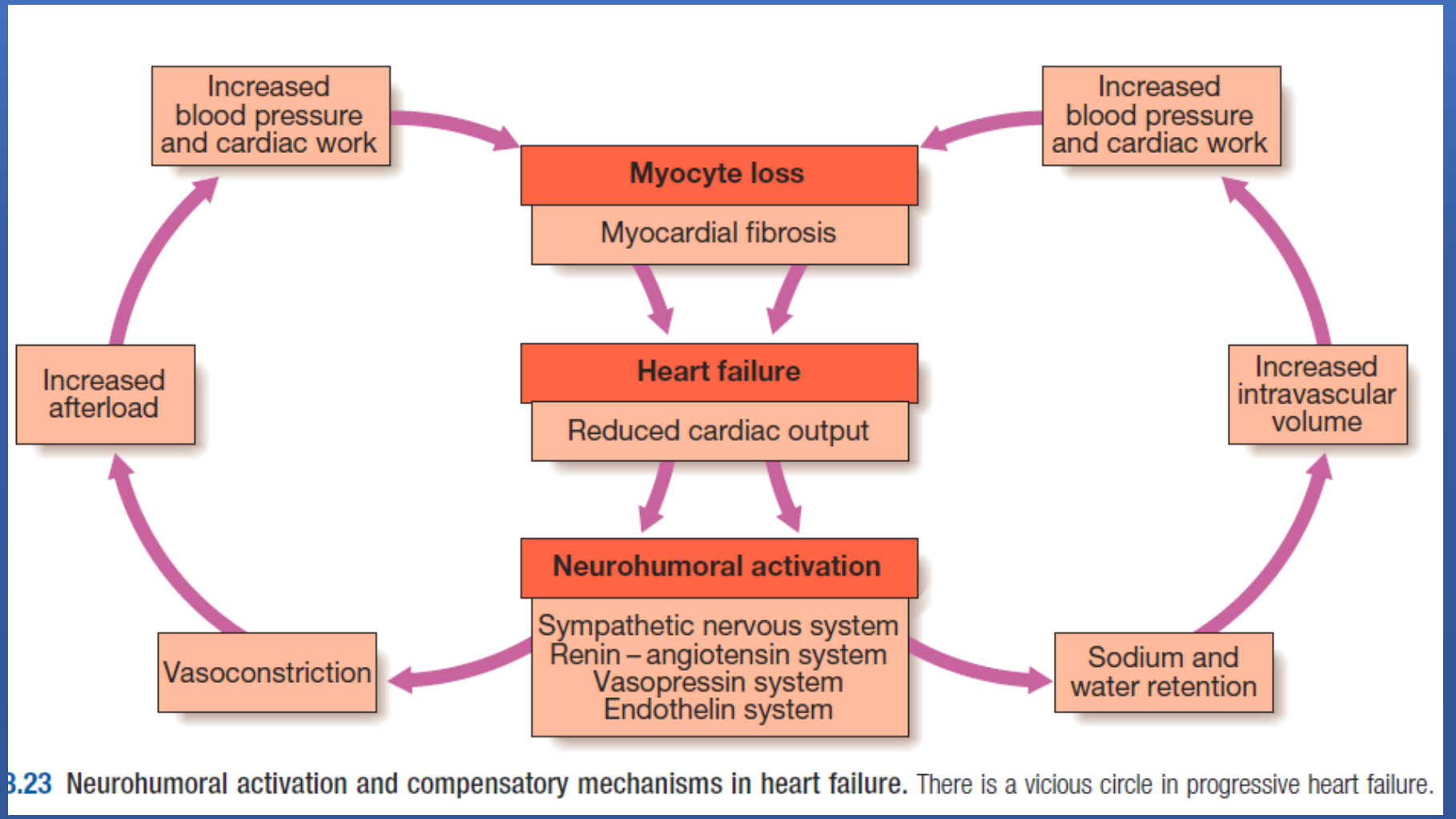
Activation of the sympathetic nervous system may initially sustain cardiac output through increased myocardial contractility (inotropy) and heart rate (chronotropy).

Prolonged sympathetic stimulation also causes negative effects, including cardiac myocyte apoptosis, hypertrophy and focal myocardial necrosis.

Sympathetic stimulation also causes peripheral vasoconstriction and arrhythmias.

Sodium and water retention is promoted by the release of aldosterone, endothelin-1 (a potent vasoconstrictor peptide with marked effects on the renal vasculature) and, in severe heart failure, antidiuretic hormone (ADH).

Natriuretic peptides are released from the atria in response to atrial stretch, and act as physiological antagonists to the fluid-conserving effect of aldosterone.



3.23 Neurohumoral activation and compensatory mechanisms in heart failure. There is a vicious circle in progressive heart failure.

Heart Failure

Pathophysiology

A. Cardiac compensatory mechanisms

1. Tachycardia
2. Ventricular dilation - Frank Starling's law
3. Myocardial hypertrophy

Heart Failure
Pathophysiology

B. *Homeostatic Compensatory Mechanisms*

Activation of Sympathetic Nervous System (First line)

1. In vascular system resulting in vasoconstriction
   (What effect on *afterload*?)
2. Kidneys
   i. Decrease renal perfusion → Renin angiotensin release
   ii. Aldosterone release → Na and H_2O retention
3. Liver
   i. Stores venous volume causing ascites, hepatomegaly

Heart Failure

Pathophysiology

Counter Regulatory Response

- Increase Na → release of Anti diuretic hormone (ADH)
- Release of atrial natriuretic factor (ANP) and BNP → Na and H_20 excretion
  - Thus ***Prevents*** severe cardiac decompensation

Heart Failure

Pathophysiology

Counter Regulatory Response

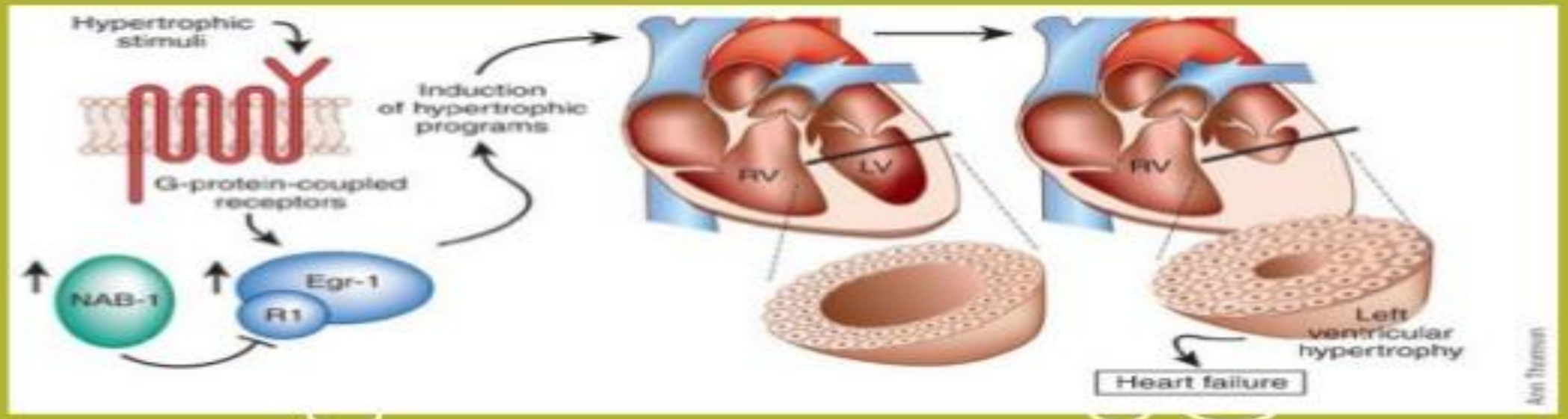
- ***Neurohormonal responses:*** *Endothelin* - stimulated by ADH, catecholamines, and angiotensin II
  - Arterial vasoconstriction
  - Increase in cardiac contractility
  - Hypertrophy

Heart Failure

Pathophysiology

Counter Regulatory Response

- ***Neurohormonal responses:*** *Proinflammatory cytokines* (e.g., tumor necrosis factor)
  - Released by cardiac myocytes in response to cardiac injury
  - Depress cardiac function → *cardiac hypertrophy, contractile dysfunction, and myocyte cell death*



Heart Failure
Pathophysiology

- ***Neurohormonal responses:*** *Over time* → systemic inflammatory response → results
  - Cardiac wasting
  - Muscle myopathy
  - Fatigue

Heart Failure
Pathophysiology

Counter Regulatory Response

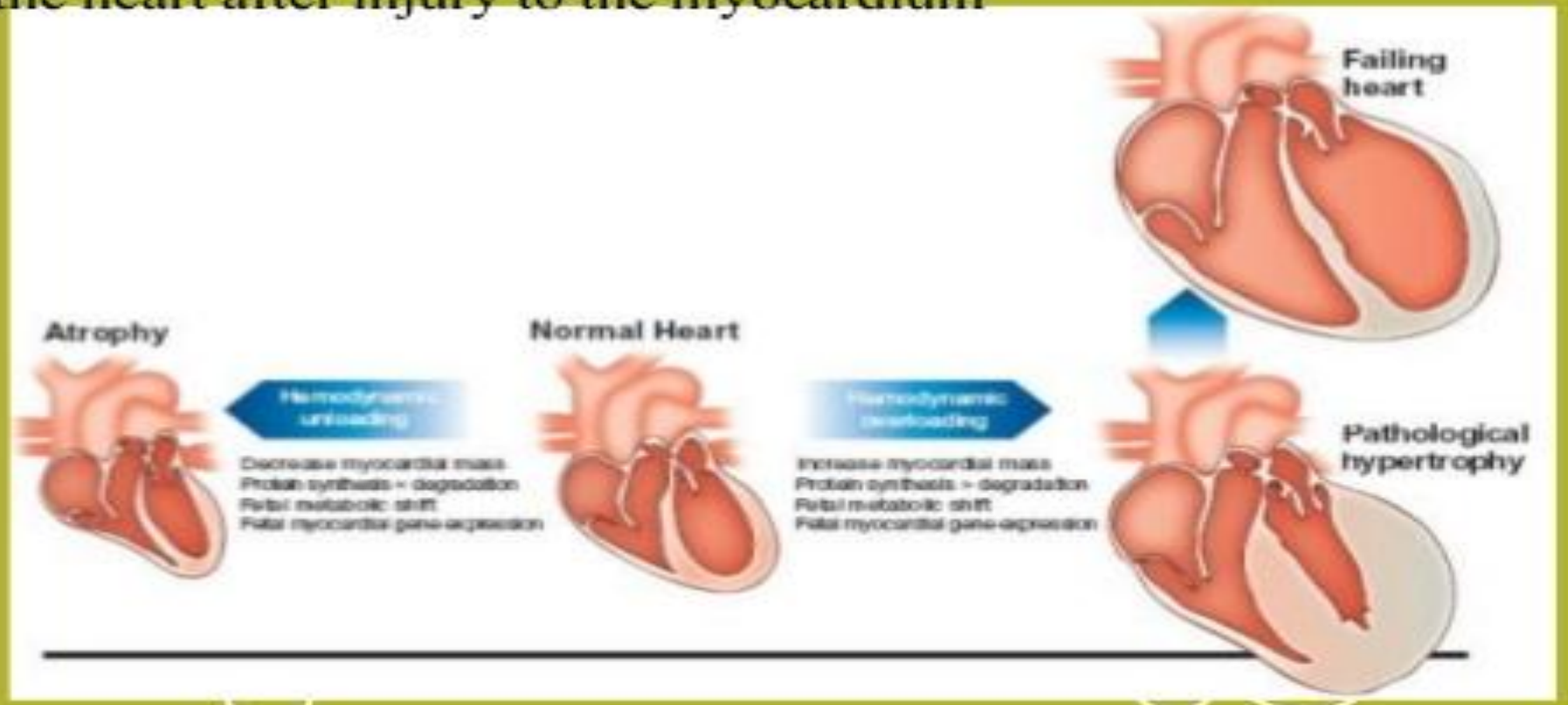
- Natriuretic peptides: atrial natriuretic peptide (ANP) and b-type natriuretic peptide (BNP)
  - Released in response to increase in atrial volume and ventricular pressure
  - Promote venous and arterial vasodilation, *reduce preload and afterload*
  - Prolonged HF → *depletion of these factors*

Heart Failure
Pathophysiology

- ***Consequences of compensatory mechanisms***
  - *Ventricular dilation:* Enlargement of heart chambers → elevated left ventricular pressure → initially effective adaptive mechanism → *then mechanism inadequate* → *cardiac output decrease*
  - *Frank-Starling law:* Initially increase venous return results in increase in force of contraction → later increase ventricular filling and myocardial stretch eventually results in *ineffective contraction*
  - *Hypertrophy:* Increase in muscle mass and cardiac wall thickness in response to chronic dilation → heart muscle poor contractility, increase in oxygen needs, poor coronary artery circulation, *prone to ventricular dysrhythmias (sudden cardiac death)*

Heart Failure
Pathophysiology

- ***Ventricular remodeling/ cardiac remodeling***
  - Refers to the changes in size, shape, structure and physiology of the heart after injury to the myocardium



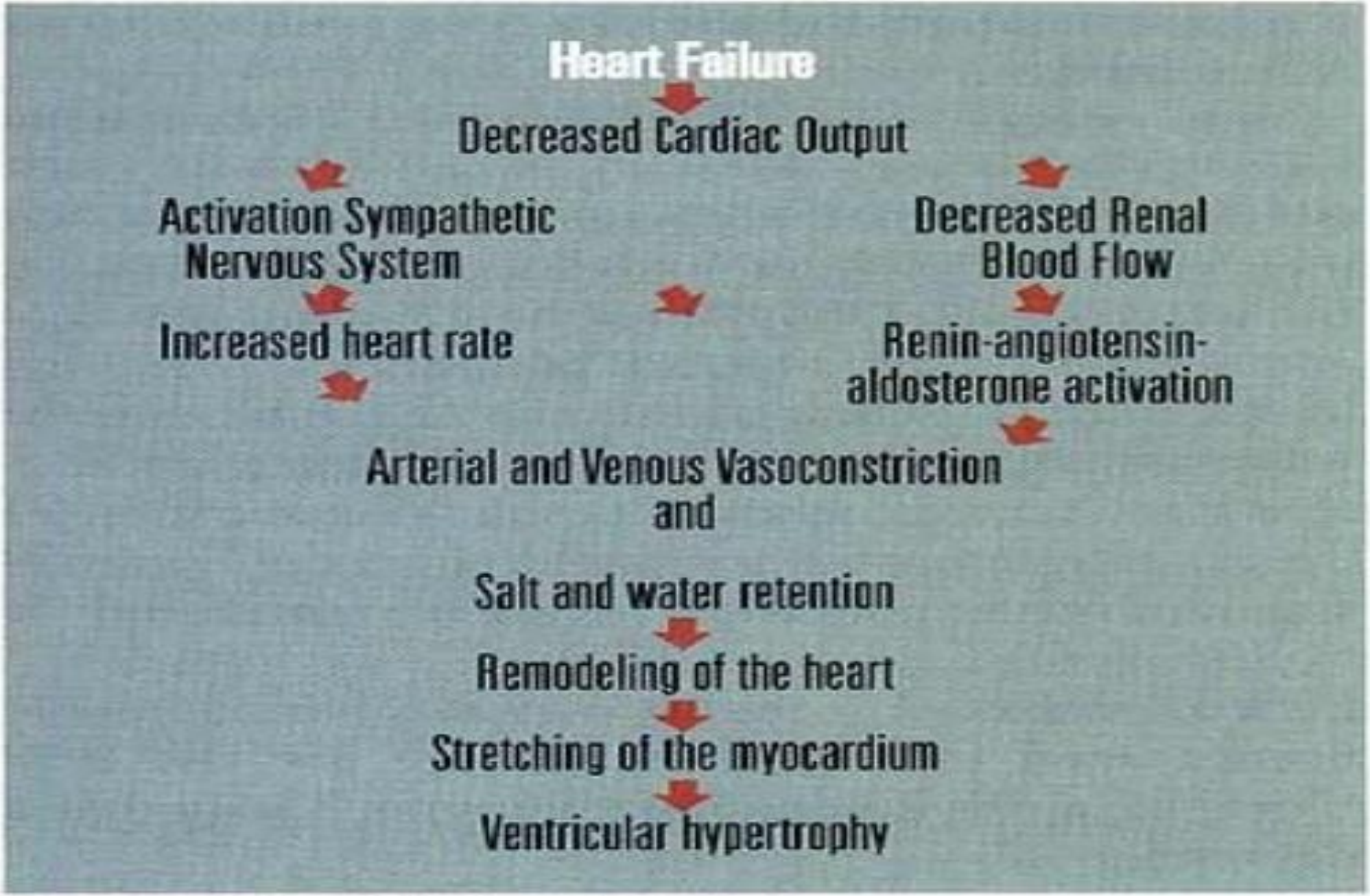


Figure 1. *Heart Failure Cycle.*

CARDIAC REMODELING

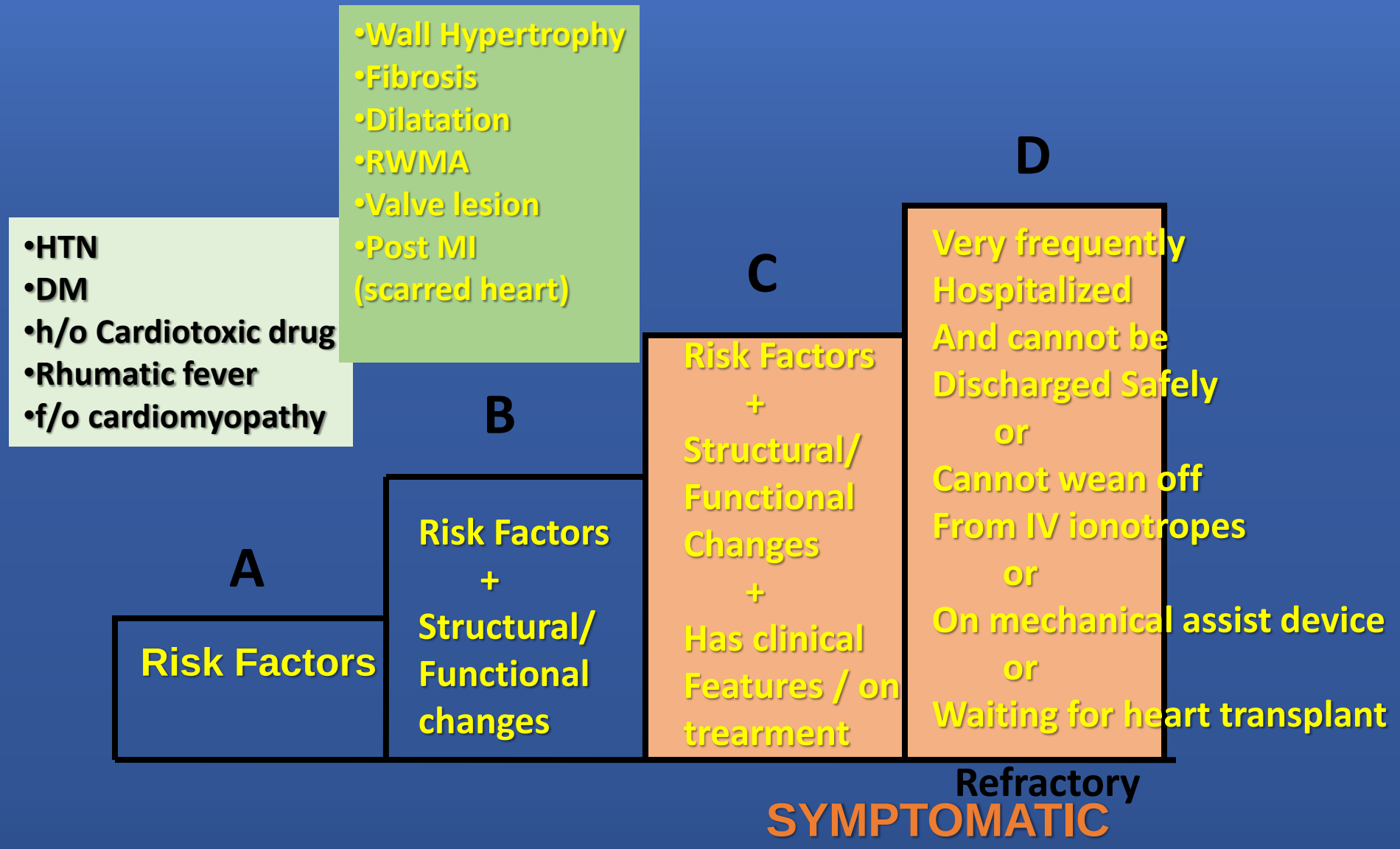
- Remodeling is defined as alteration in the structure (dimensions, mass, shape) of the heart in response to hemodynamic load and/or cardiac injury in association with neurohormonal activation.
- Remodeling may be described as physiologic or pathologic; alternatively, remodeling may be classified as adaptive or maladaptive
- Whereas neurohormonal antagonists stabilize HF and in some cases reverse certain aspects of the disease process, HF will progress in the overwhelming majority of patients, albeit at a slower rate.
- It has recently been suggested that the process of LV remodeling is directly related to future deterioration in LV performance and a less favorable clinical course in patients with HF.

NYHA Class and Mortality

NYHA Class	1-Yr Mortality
Class I Asymptomatic: No limitation of physical activity. Ordinary activity does not cause sxs.	5-10%
II Symptomatic with moderate exertion. Ordinary physical activity causes SOB, fatigue	5-10%
III Symptomatic with minimal exertion. Less than usual activity causes sxs	10-25%
IV Symptomatic at rest. Unable to carry on any activity without discomfort.	25-60%

ACC/AHA Guidelines 2013

ACC/AHA stages of Heart Failure



Classification of Heart Failure: ACC/AHA Stage vs NYHA Class

ACC/AHA Heart Failure Stage	NYHA Functional Class
A. At risk for heart failure but without structural heart disease or symptoms	None
B. Structural heart disease but without heart failure	I. Asymptomatic
C. Structural heart disease with prior or current heart failure symptoms	II. Symptomatic with moderate exertion III. Symptomatic with minimal exertion
D. Refractory heart failure requiring specialized interventions	IV. Symptomatic at rest

Hunt SA et al. *Circulation*. 2001;104:2996-3007.
Farrell MH et al. *JAMA*. 2002;287:890-897.

Types of heart failure

Left, right and biventricular heart failure

- Left-sided heart failure.

- Right-sided heart failure.

- Biventricular heart failure.

Diastolic and systolic dysfunction :

Heart failure may develop as a result of impaired myocardial contraction (systolic dysfunction) but can also be due to poor ventricular filling and high filling pressures stemming from abnormal ventricular relaxation (diastolic dysfunction).

The latter is caused by a stiff, noncompliant ventricle and is commonly found in patients with left ventricular hypertrophy.

Systolic and diastolic dysfunction often coexist, particularly in patients with coronary artery disease.

High-output failure

A large arteriovenous shunt, beri-beri, severe anaemia or thyrotoxicosis can occasionally cause heart failure due to an excessively high cardiac output.

18.12 Factors that may precipitate or aggravate heart failure in pre-existing heart disease

- Myocardial ischaemia or infarction
- Intercurrent illness, e.g. infection
- Arrhythmia, e.g. atrial fibrillation
- Inappropriate reduction of therapy
- Administration of a drug with negative inotropic (β-blocker) or fluid-retaining properties (NSAIDs, corticosteroids)
- Pulmonary embolism
- Conditions associated with increased metabolic demand, e.g. pregnancy, thyrotoxicosis, anaemia
- IV fluid overload, e.g. post-operative IV infusion

(NSAIDs = non-steroidal anti-inflammatory drugs)

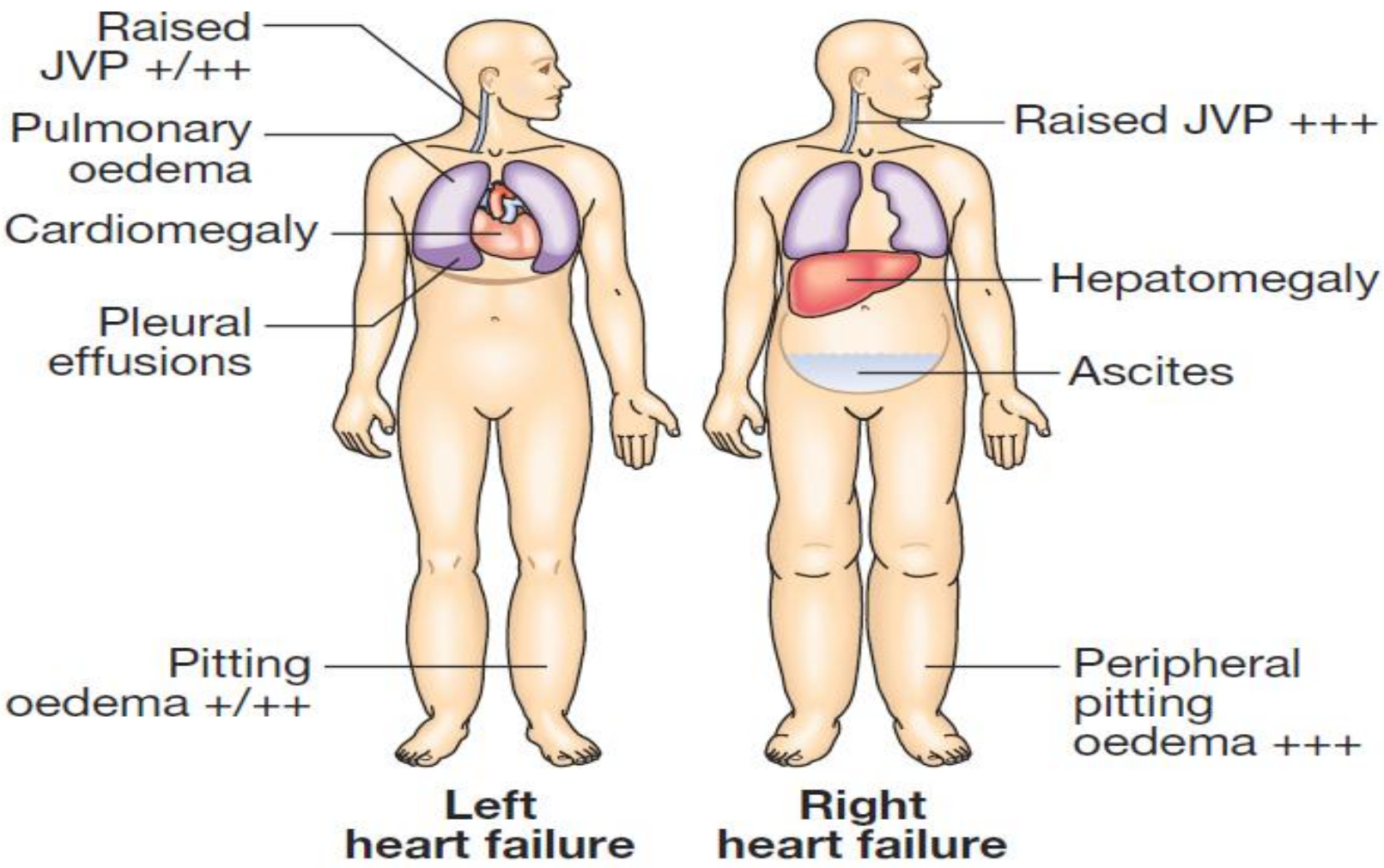


Fig. 18.24 Clinical features of left and right heart failure.
(JVP = jugular venous pressure)

Low cardiac output causes fatigue, listlessness and a poor effort tolerance; the peripheries are cold and the BP is low.

To maintain perfusion of vital organs, blood flow is diverted away from skeletal muscle and this may contribute to fatigue and weakness.

Poor renal perfusion leads to oliguria and uraemia.

Chronic heart failure is sometimes associated with marked weight loss (cardiac cachexia), caused by a combination of anorexia and impaired absorption due to gastrointestinal congestion, poor tissue perfusion due to a low cardiac output, and skeletal muscle atrophy due to immobility.

Acute Decompensated Heart Failure (ADHF)

Clinical Manifestations

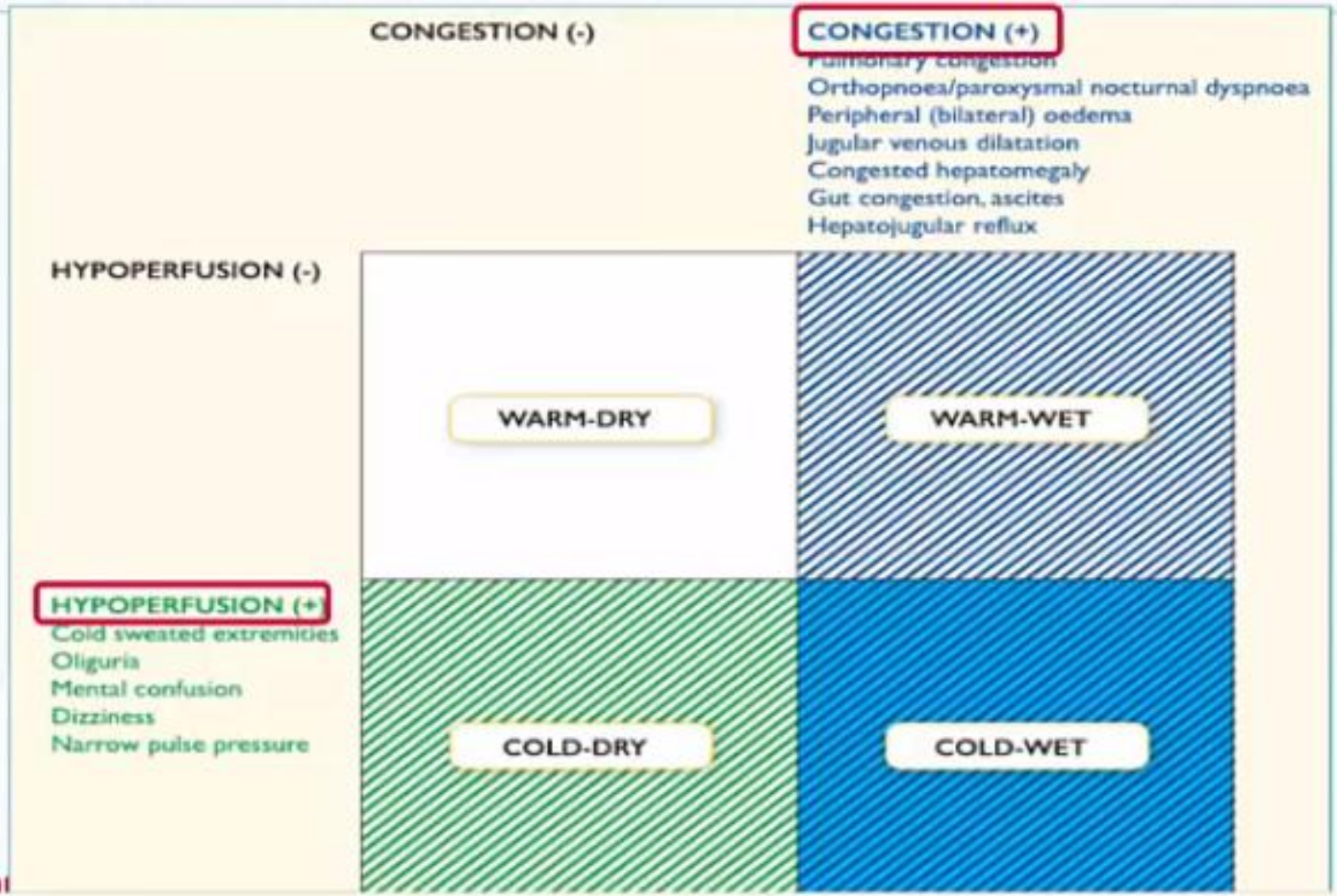
Physical findings

- Orthopnea
- Dyspnea, Tachypnea
- Use of accessory muscles of respiration
- Cyanosis
- Cool and clammy skin
- S3 gallop rhythm

Physical findings

- Cough with frothy, blood-tinged sputum
- Breath sounds: Crackles, wheezes, rhonchi
- Tachycardia
- Hypotension or hypertension

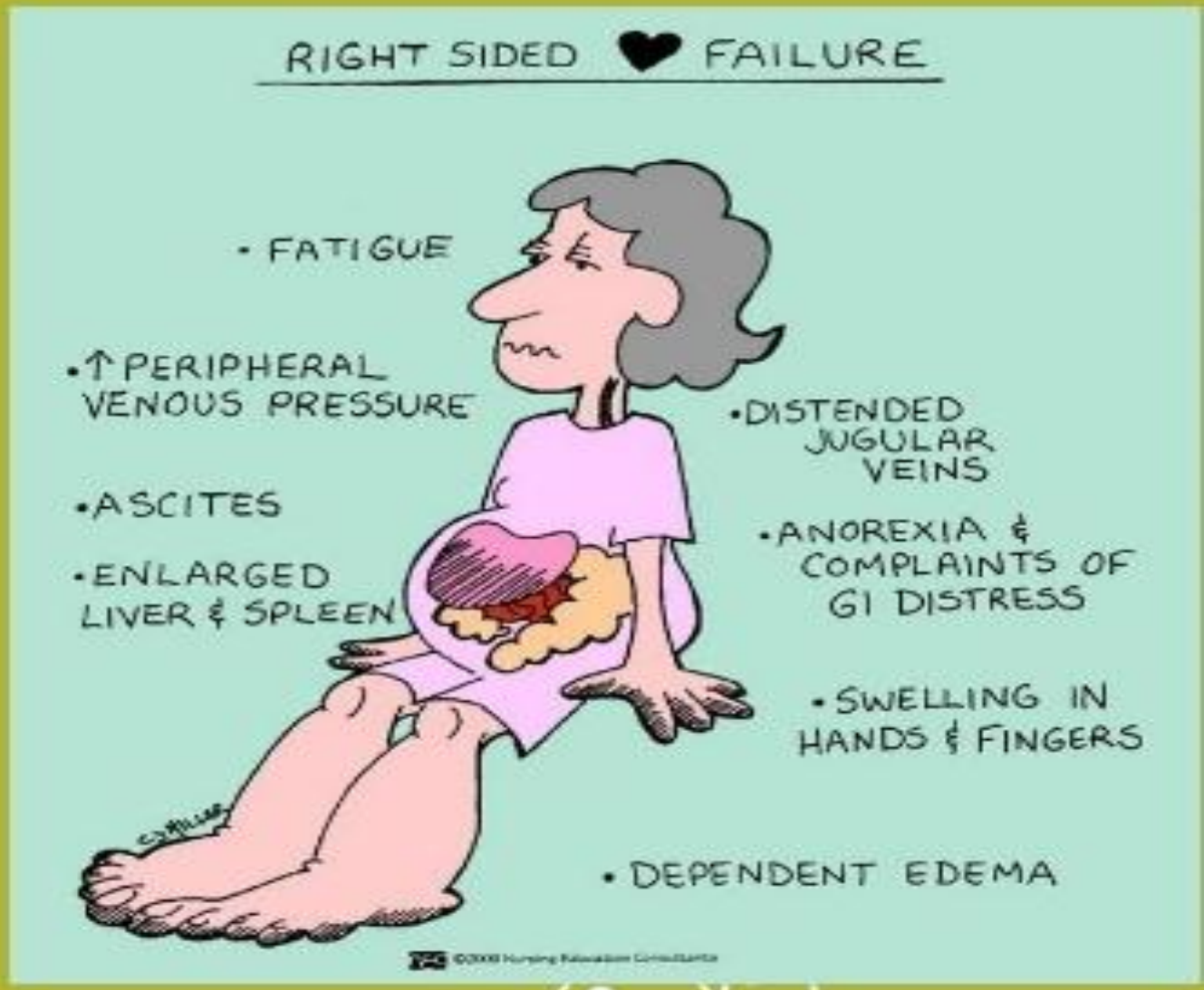
Clinical profiles of patients with acute HF based on the presence/absence of congestion and/or hypoperfusion



Hypoperfusion is not synonymous with hypotension, but often hypoperfusion is accompanied by hypotension.

Right Heart Failure

- ***Signs and Symptoms***
  - Fatigue, weakness, lethargy
  - weight gain
  - Increase abdominal girth
  - Anorexia
  - Right upper quadrant pain
  - elevated neck veins
  - Hepatomegaly
  - May not see signs of LVF



Complications

In advanced heart failure, the following may occur:

1- Renal failure is caused by poor renal perfusion due to low cardiac output and may be exacerbated by diuretic therapy, angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers.

2- Hypokalaemia may be the result of treatment with potassium-losing diuretics or hyperaldosteronism caused by activation of the renin–angiotensin system and impaired aldosterone metabolism due to hepatic congestion.

Most of the body's potassium is intracellular and there may be substantial depletion of potassium stores, even when the plasma concentration is in the reference range.

3- Hyperkalaemia may be due to the effects of drugs which promote renal resorption of potassium, in particular the combination of ACE inhibitors (or angiotensin receptor blockers) and mineralocorticoid receptor antagonists. These effects are amplified if there is renal dysfunction due to low cardiac output or atherosclerotic renal vascular disease.

4- *Hyponatraemia* is a feature of severe heart failure and is a poor prognostic sign. It may be caused by diuretic therapy, inappropriate water retention due to high ADH secretion, or failure of the cell membrane ion pump.

5- *Impaired liver function* is caused by hepatic venous congestion and poor arterial perfusion, which frequently cause mild jaundice and abnormal liver function tests; reduced synthesis of clotting factors can make anticoagulant control difficult.

6- Thromboembolism. Deep vein thrombosis and pulmonary embolism may occur due to the effects of a low cardiac output and enforced immobility. Systemic emboli occur in patients with atrial fibrillation or flutter, or with intracardiac thrombus complicating conditions such as mitral stenosis, MI or left ventricular aneurysm.

7- *Atrial and ventricular arrhythmias* are very common and may be related to electrolyte changes (e.g. hypokalaemia, hypomagnesaemia), the underlying cardiac disease, and the pro-arrhythmic effects of sympathetic activation. Atrial fibrillation occurs in approximately 20% of patients with heart failure and causes further impairment of cardiac function. Sudden death occurs in up to 50% of patients with heart failure and is often due to a ventricular arrhythmia. Frequent ventricular ectopic beats and runs of non-sustained ventricular tachycardia are common findings in patients with heart failure and are associated with an adverse prognosis.

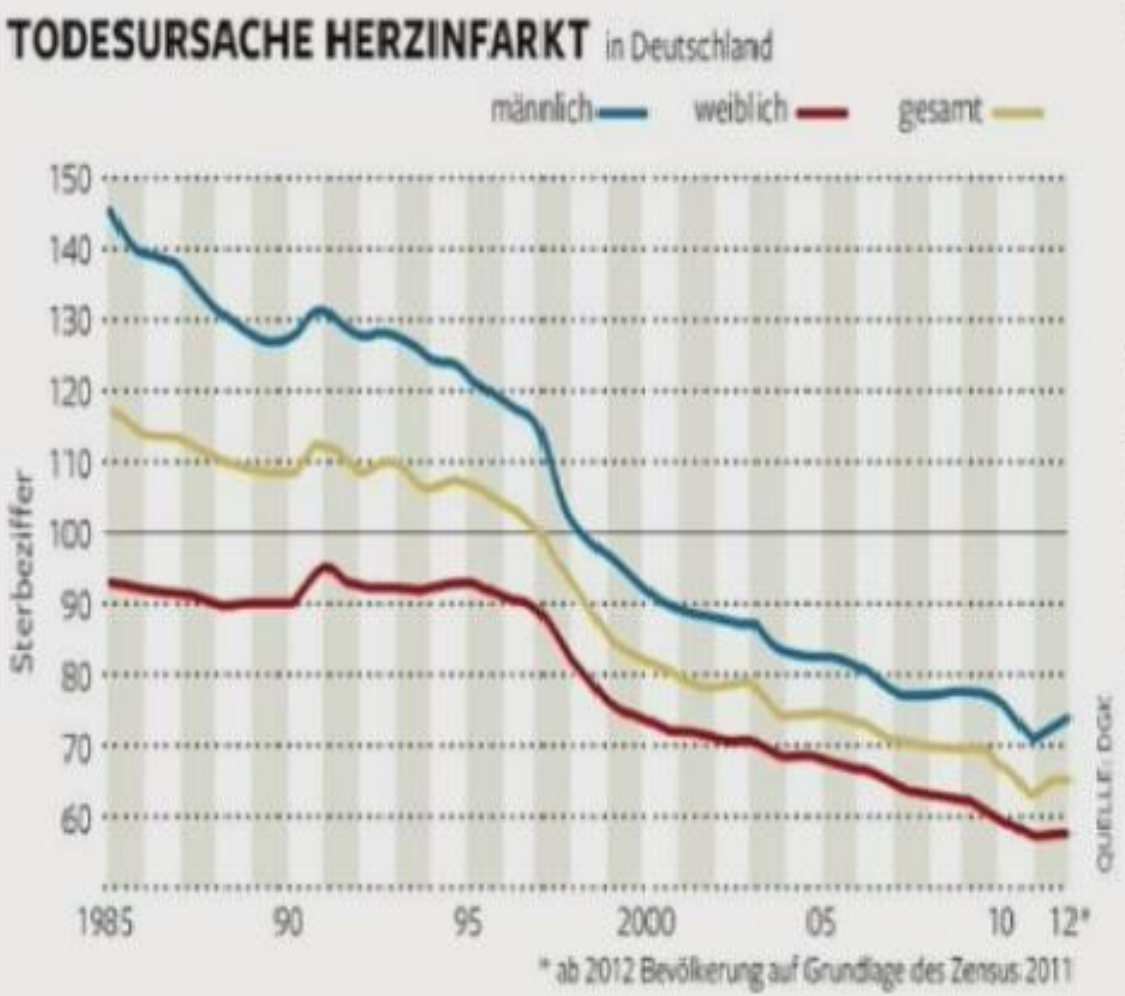
Clinical Framingham Heart Study criteria for Heart failure

Major Criteria	Minor Criteria
Paroxysmal nocturnal dyspnea or orthopnea	Dyspnea on exertion
Elevated jugular venous pressure	Night cough
Hepatojugular reflux	Tachycardia > 120 bpm
Pulmonary rales	Hepatomegaly
S_3 gallop	Bilateral lower extremity edema
Enlarging heart silhouette on consecutive chest x-rays	Pulmonary vascular engorgement on chest x-ray
Pulmonary edema on chest x-ray	Pleural effusion on chest x-ray
Weight loss on diuretics (> 10 lb in 5 days)	
Increased venous pressure > 16 cm H_2O (assessed via a central line)	

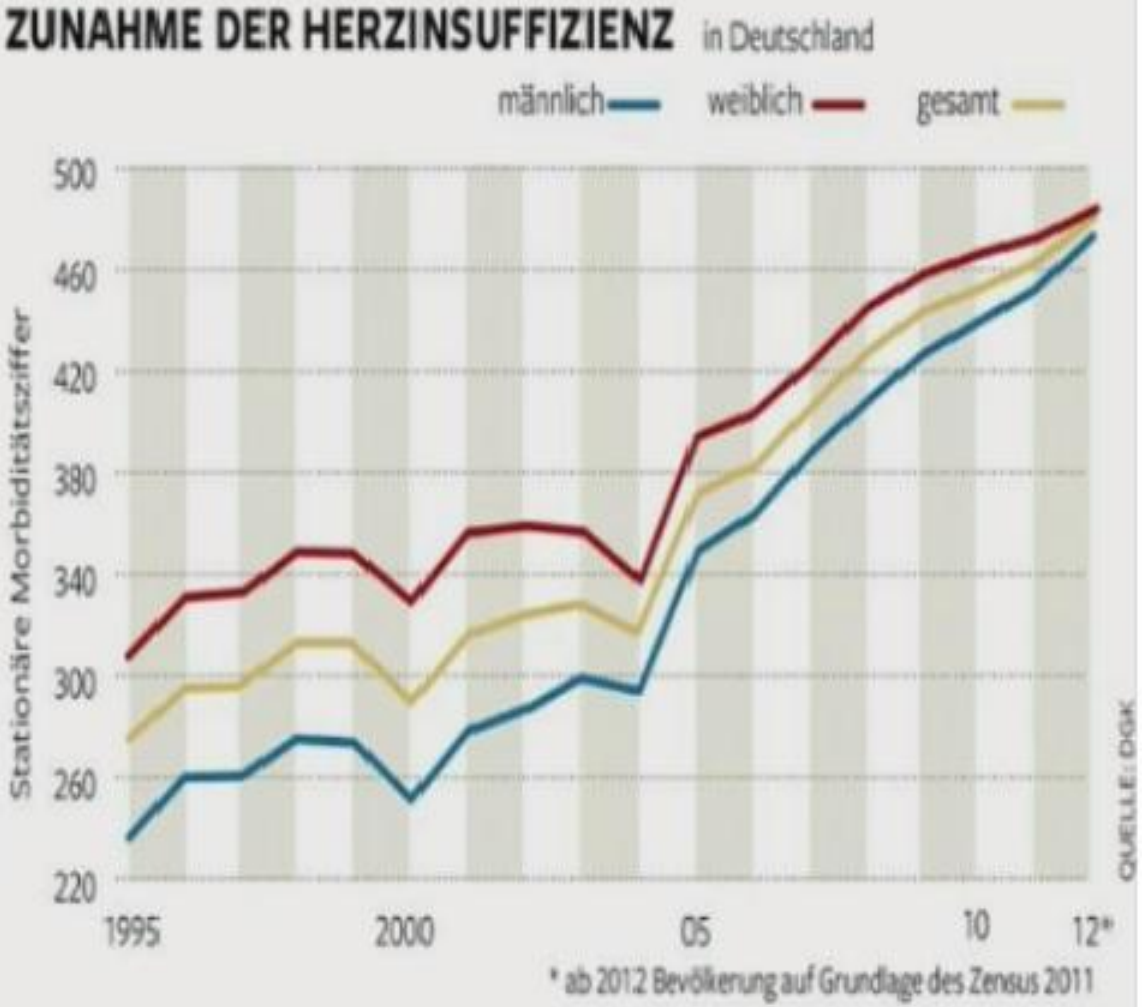
Presence of two major or one major and two minor criteria is required for heart failure diagnosis.

Heart Failure is Moving Center Stage

Fatal MI



Heart Failure



Investigations :

. Serum urea, creatinine and electrolytes.

.Haemoglobin.

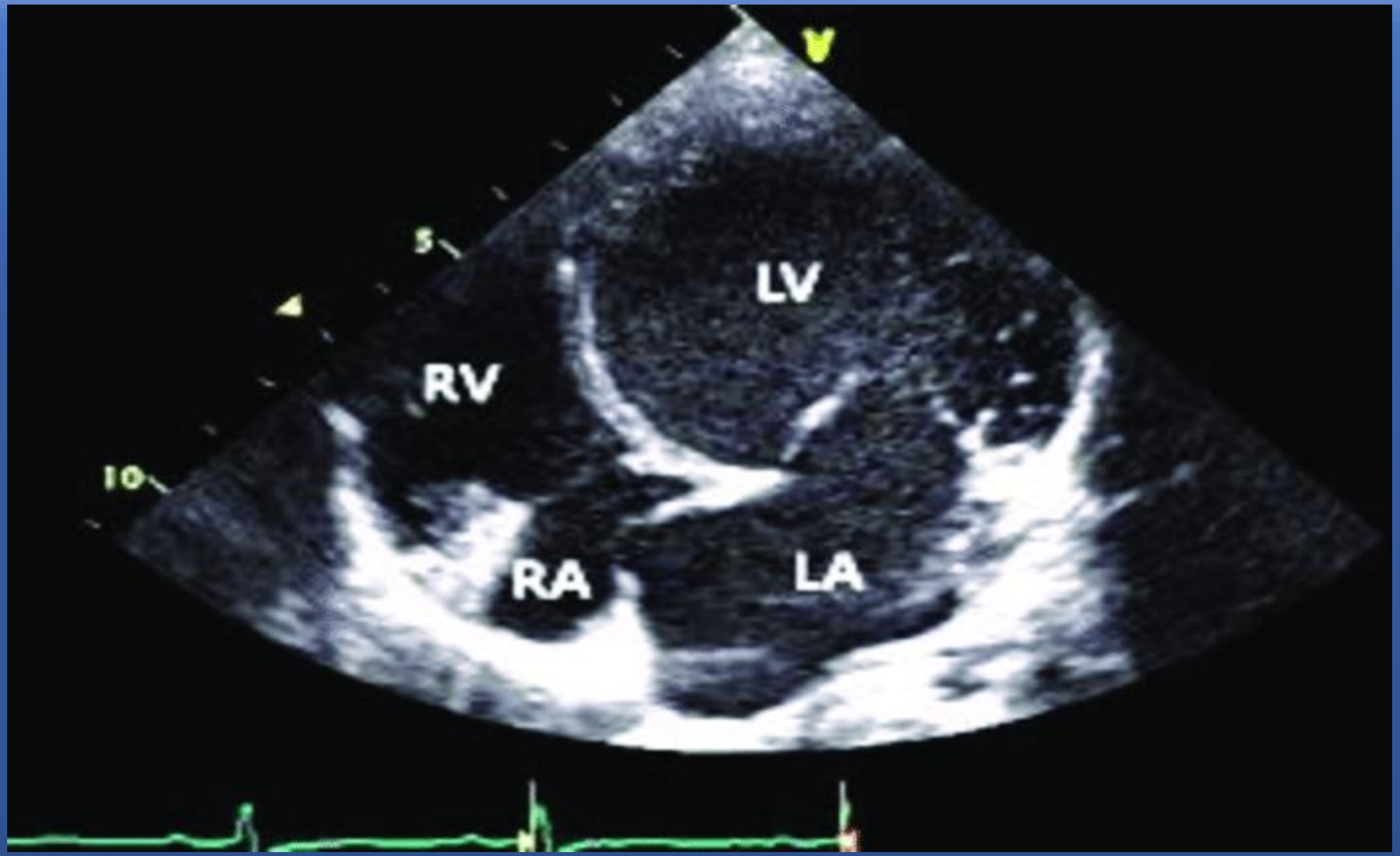
.Thyroid function.

.ECG and chest X-ray may help to establish the nature and severity of the underlying heart disease and detect any complications.

. Brain natriuretic peptide (BNP) is elevated in heart failure and is a marker of risk; it is useful in the investigation of patients with breathlessness or peripheral oedema.

.Echocardiography is very useful and should be considered in all patients with heart failure in order to:

- Determine the aetiology.
- Detect unsuspected valvular heart disease, such as occult mitral stenosis, and other conditions
- Identify patients who will benefit from long-term drug therapy, e.g. ACE inhibitors .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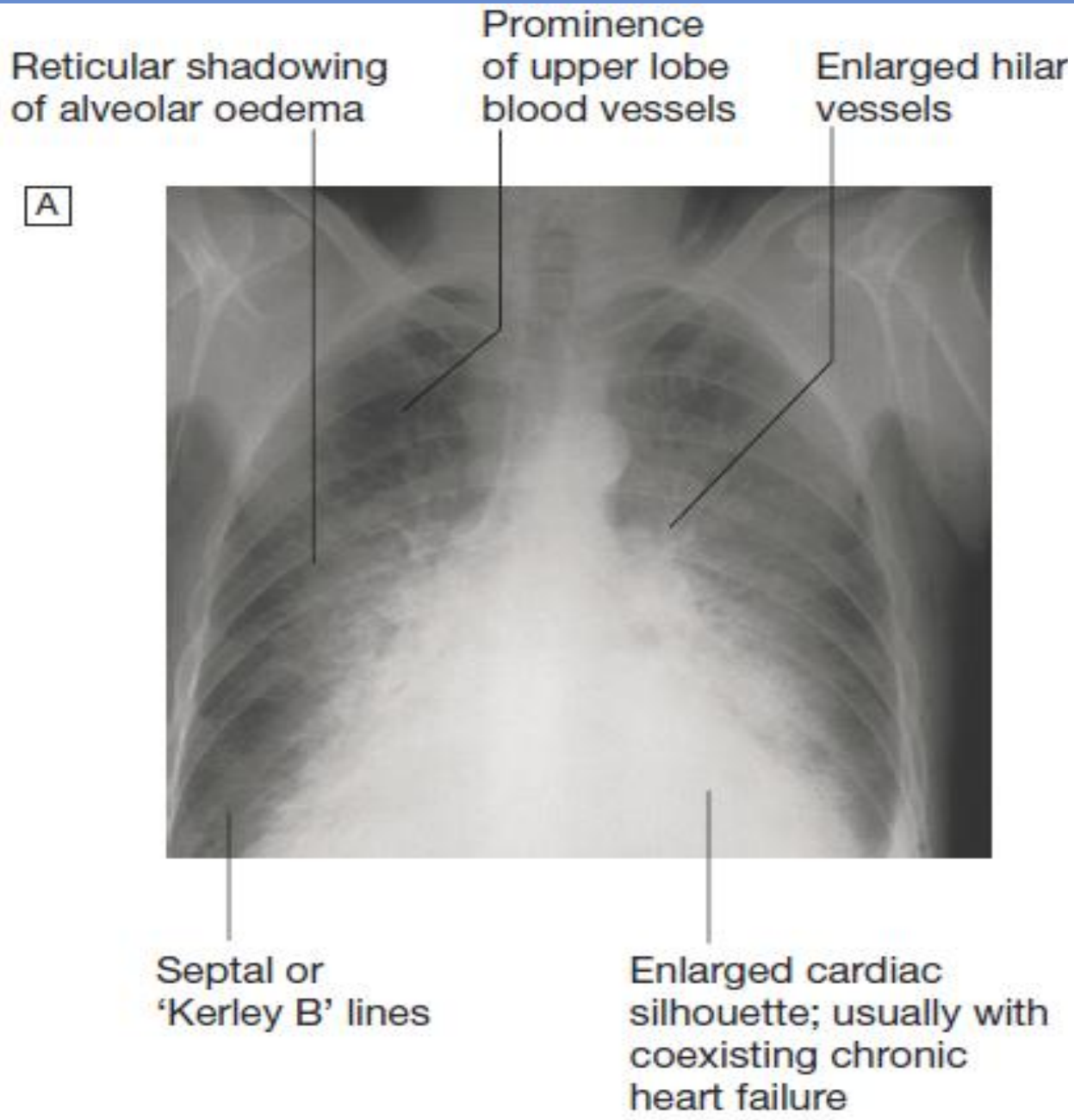
10
LV
RV
RA
LA



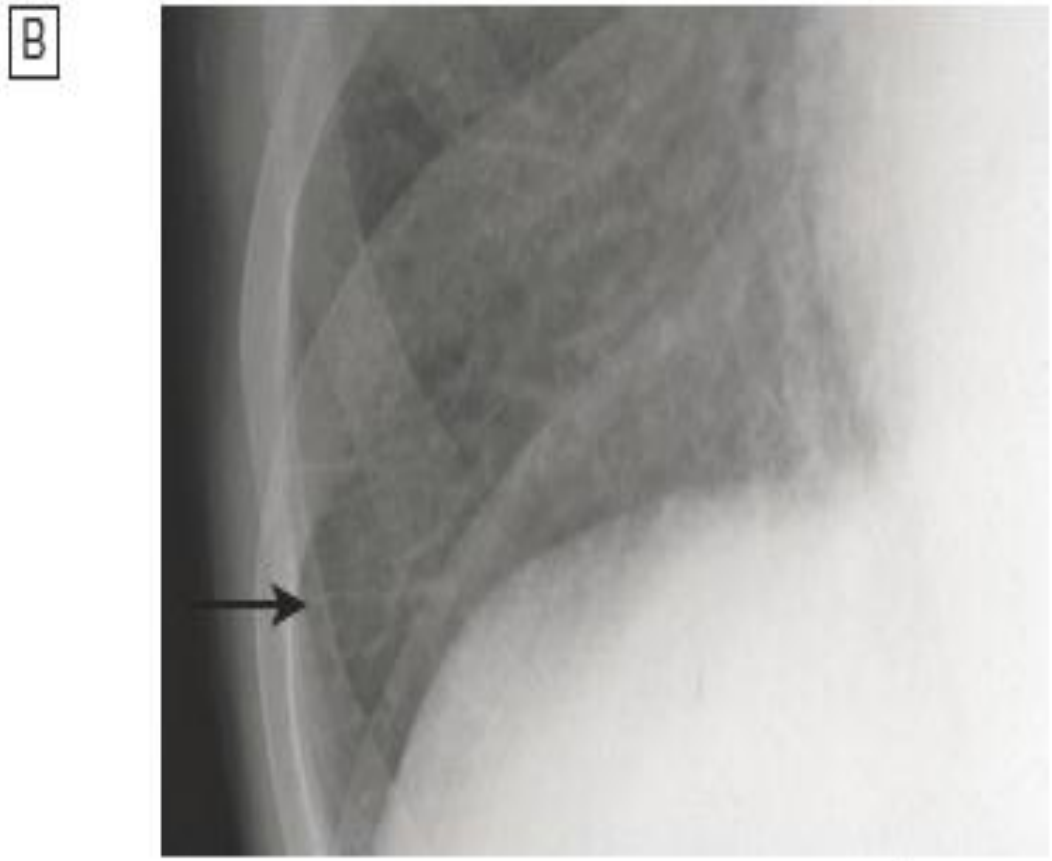


Fig. 18.25 Radiological features of heart failure. A Chest X-ray of a patient with pulmonary oedema. B Enlargement of lung base showing septal or 'Kerley B' lines (arrow).

Chest X-ray

High pulmonary venous pressure in left-sided heart failure first shows on the chest X-ray as an abnormal distension of the upper lobe pulmonary veins (with the patient in the erect position). The vascularity of the lung fields becomes more prominent, and the right and left pulmonary arteries dilate. Subsequently, interstitial oedema causes thickened interlobular septa and dilated lymphatics. These are evident as horizontal lines in the costophrenic angles (septal or 'Kerley B' lines). More advanced changes due to alveolar oedema cause a hazy opacification spreading from the hilar regions, and pleural effusions.

Management of acute pulmonary oedema

This is an acute medical emergency:

- Sit the patient up to reduce pulmonary congestion.
- Give oxygen (high-flow, high-concentration). Non-invasive positive pressure ventilation (continuous positive airways pressure (CPAP) of 5–10 mmHg) by a tight-fitting facemask results in a more rapid clinical improvement.
- Administer nitrates, such as IV glyceryl trinitrate (10–200 µg/min or buccal glyceryl trinitrate 2–5 mg, titrated upwards every 10 minutes), until clinical improvement occurs or systolic BP falls to less than 110 mmHg.
- Administer a loop diuretic, such as furosemide (50–100 mg IV).

The patient should initially be kept rested, with continuous monitoring of cardiac rhythm, BP and pulse oximetry.

… Intravenous opiates must be used sparingly in distressed patients, as they may cause respiratory depression and exacerbation of hypoxaemia and hypercapnia.

If these measures prove ineffective, inotropic agents may be required to augment cardiac output, particularly in hypotensive patients. Insertion of an intra-aortic balloon pump may be beneficial in patients with acute cardiogenic pulmonary oedema and shock.

Management of chronic heart failure

General measures

18.14 General measures for the management of heart failure

Education
• Explanation of nature of disease, treatment and self-help strategies
Diet
• Good general nutrition and weight reduction for the obese • Avoidance of high-salt foods and added salt, especially for patients with severe congestive heart failure
Alcohol
• Moderation or elimination of alcohol consumption. Alcohol-induced cardiomyopathy requires abstinence
Smoking
• Cessation
Exercise
• Regular moderate aerobic exercise within limits of symptoms
Vaccination
• Consider influenza and pneumococcal vaccination

Diuretic therapy

In heart failure, diuretics produce an increase in urinary sodium and water excretion, leading to reduction in blood and plasma volume . Diuretic therapy reduces preload and improves pulmonary and systemic venous congestion.

It may also reduce afterload and ventricular volume, leading to a fall in ventricular wall tension and increased cardiac efficiency.

Although a fall in preload (ventricular filling pressure) tends to reduce cardiac output, the ‘Starling curve’ in heart failure is flat, so there may be a substantial and beneficial fall in filling pressure with little change in cardiac output . Nevertheless, excessive diuretic therapy may cause an undesirable fall in cardiac output, especially in patients with a marked diastolic component to their heart failure. This leads to hypotension, lethargy and renal failure.

In some patients with severe chronic heart failure, particularly if there is associated renal impairment, oedema may persist, despite oral loop diuretic therapy. In such patients, an intravenous infusion of furosemide (5–10 mg/hr) may initiate a diuresis. Combining a loop diuretic with a thiazide diuretic (e.g. Bendroflumethiazide 5 mg daily) may prove effective, but this can cause an excessive diuresis.

Mineralocorticoid receptor antagonists, such as spironolactone and eplerenone, are potassium-sparing diuretics that are of particular benefit in patients with heart failure with severe left ventricular systolic dysfunction.

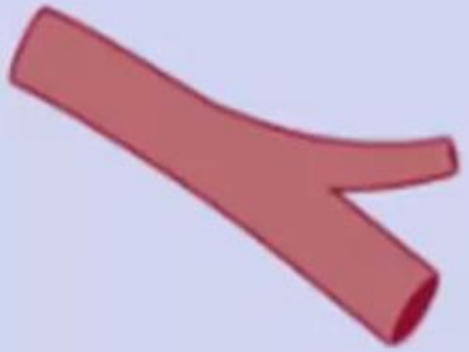
They may cause hyperkalaemia, particularly when used with an ACE inhibitor.

They improve longterm clinical outcome in patients with severe heart failure or heart failure following acute MI.

Sympathetic nervous system

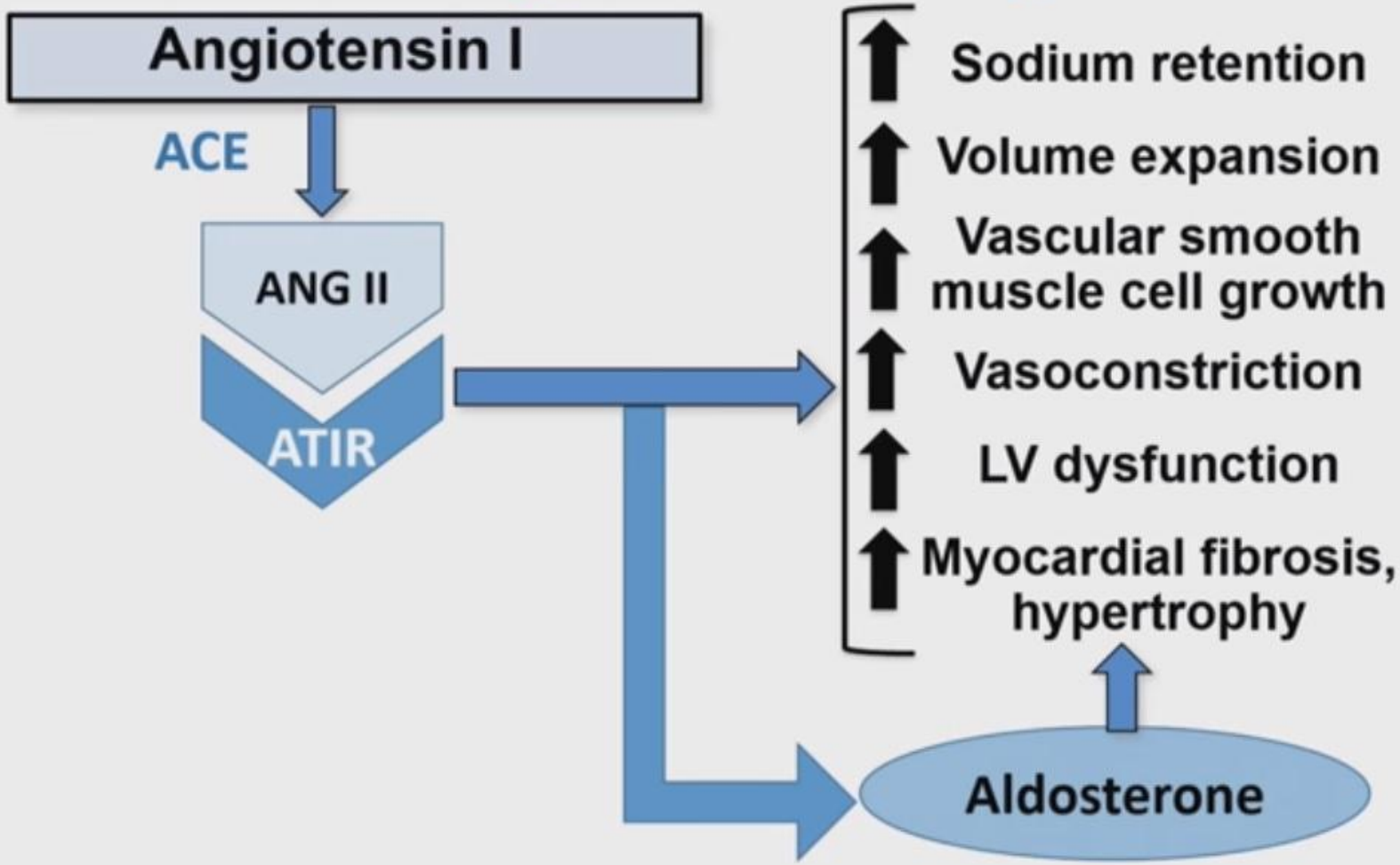
↓β–AR responsiveness
Myocyte hypertrophy
Myocyte necrosis and apoptosis, fibrosis
↓Norepinephrine stores
↓Sympathetic innervation
Arrhythmias
Impaired diastolic, systolic function

↑Tubular reabsorption of Na^+
Activation of RAS
↑Renal vascular resistance
↓Response to natriuretic factors
↑Renin release



Neurogenic vacoconstriction
Vascular hypertrophy

Renin Angiotensin System



Angiotensin-converting enzyme inhibition therapy

-Angiotensin-converting enzyme (ACE) inhibition therapy interrupts the vicious circle of neurohumoral activation that is characteristic of moderate and severe heart failure by preventing the conversion of angiotensin I to angiotensin II, thereby preventing peripheral vasoconstriction, activation of the sympathetic nervous system , and salt and water retention due to aldosterone release. These drugs also prevent the undesirable activation of the renin–angiotensin system caused by diuretic therapy.

- In moderate and severe heart failure, ACE inhibitors can produce a substantial improvement in effort tolerance and in mortality.

- They can also improve outcome and prevent the onset of overt heart failure in patients with poor residual left ventricular function following MI .

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They can also improve outcome and prevent the onset of overt heart failure in patients with poor residual left ventricular function following MI .

ACE inhibitors can cause symptomatic hypotension and impairment of renal function, especially in patients with bilateral renal artery stenosis or those with preexisting renal disease.

An increase in serum potassium concentration may occur that can offset hypokalaemia associated with loop diuretic therapy.

Short-acting ACE inhibitors can cause marked falls in BP, particularly in the elderly or when started in the presence of hypotension, hypovolaemia or hyponatraemia.

In stable patients without hypotension (systolic BP over 100 mmHg), ACE inhibitors can usually be safely started in the community.

However, in other patients, it is usually advisable to withhold diuretics for 24 hours before starting treatment with a small dose of a long-acting agent, preferably given at night .

Renal function and serum potassium must be monitored and should be checked 1–2 weeks after starting therapy.

Angiotensin receptor blocker therapy

Angiotensin receptor blockers act by blocking the action of angiotensin II on the heart, peripheral vasculature and kidney. In heart failure, they produce beneficial haemodynamic changes that are similar to the effects of ACE inhibitors but are generally better tolerated. They have comparable effects on mortality and are a useful alternative for patients who cannot tolerate ACE inhibitors .

Unfortunately, they share all the more serious adverse effects of ACE inhibitors, including renal dysfunction and hyperkalaemia.

ARBs are normally used as an alternative to ACE inhibitors.

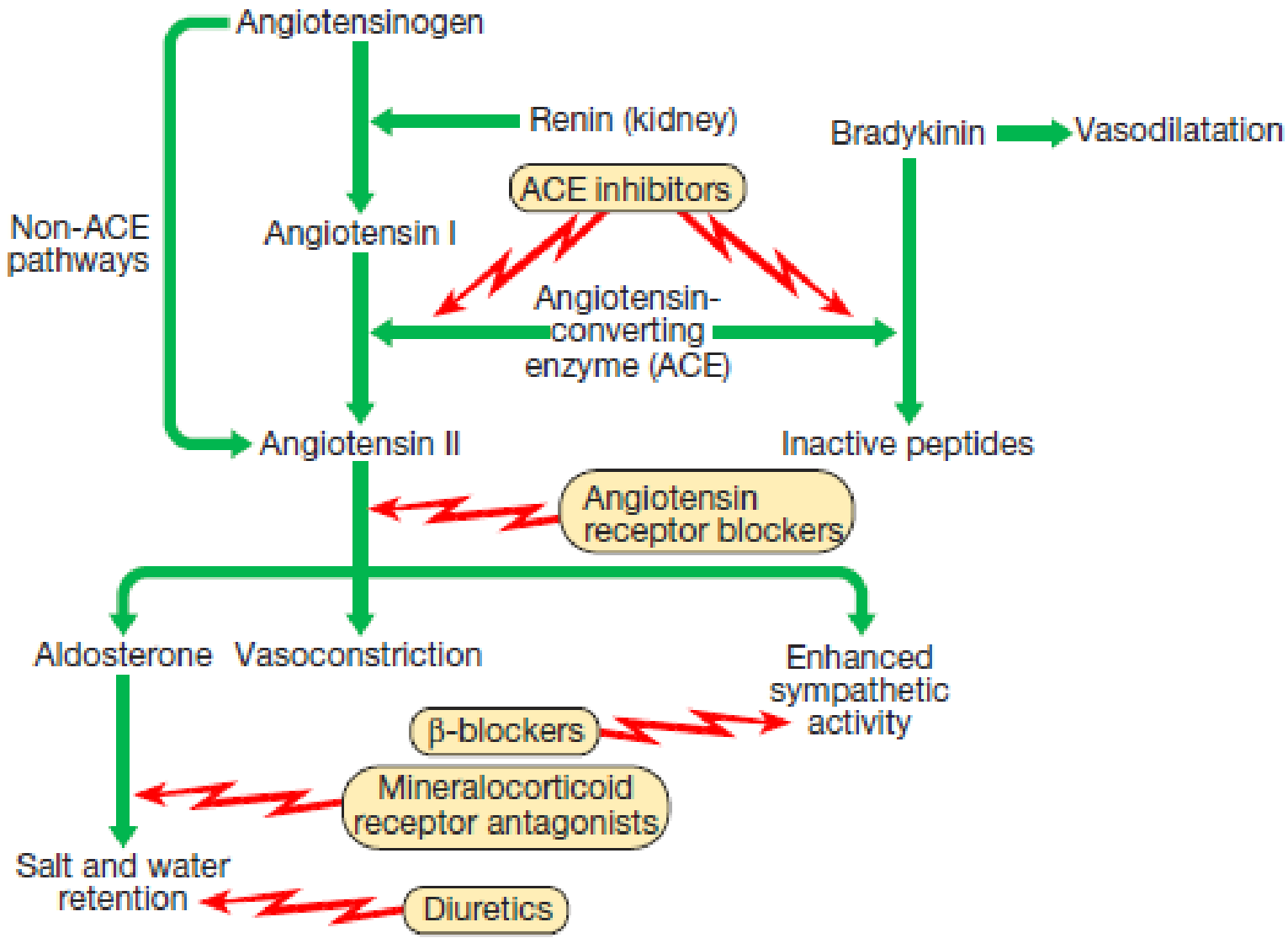


Fig. 18.27 Neurohumoral activation and sites of action of drugs used in the treatment of heart failure.

Vasodilator therapy

These drugs are valuable in chronic heart failure, when ACE inhibitor or ARB drugs are contraindicated (e.g. in severe renal failure).

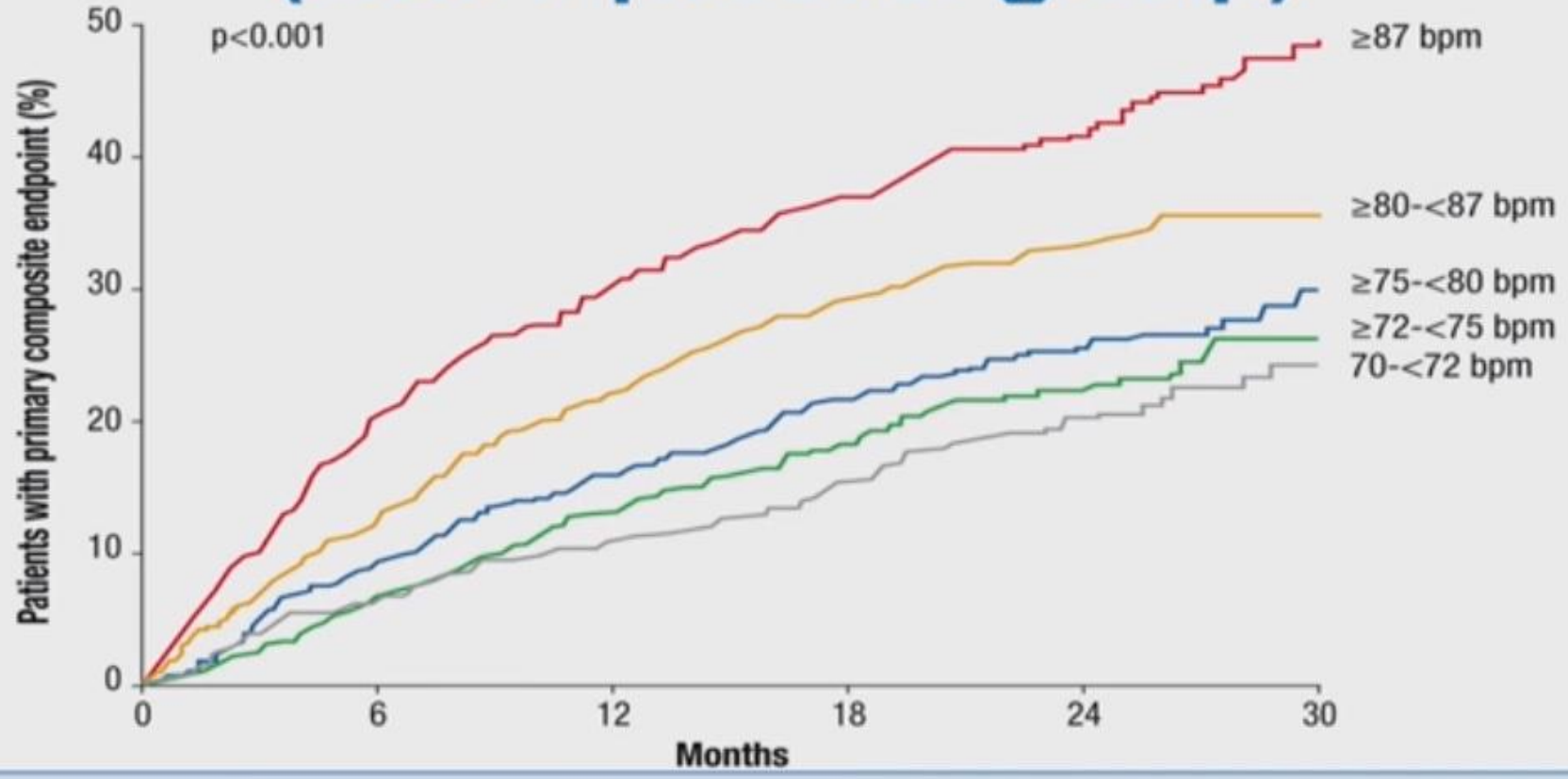
Venodilators, such as nitrates, reduce preload, and arterial dilators, such as hydralazine, reduce afterload . Their use is limited by pharmacological tolerance and hypotension.

Beta-adrenoceptor blocker therapy

Beta-blockade helps to counteract the deleterious effects of enhanced sympathetic stimulation and reduces the risk of arrhythmias and sudden death. When initiated in standard doses, they may precipitate acute-on-chronic heart failure, but when given in small incremental doses (e.g. bisoprolol started at a dose of 1.25 mg daily, and increased gradually over a 12-week period to a target maintenance dose of 10 mg daily), they can increase ejection fraction, improve symptoms, reduce the frequency of hospitalisation and reduce mortality in patients with chronic heart failure .

Betablockers are more effective at reducing mortality than ACE inhibitors: relative risk reduction of 33% versus 20%, respectively.

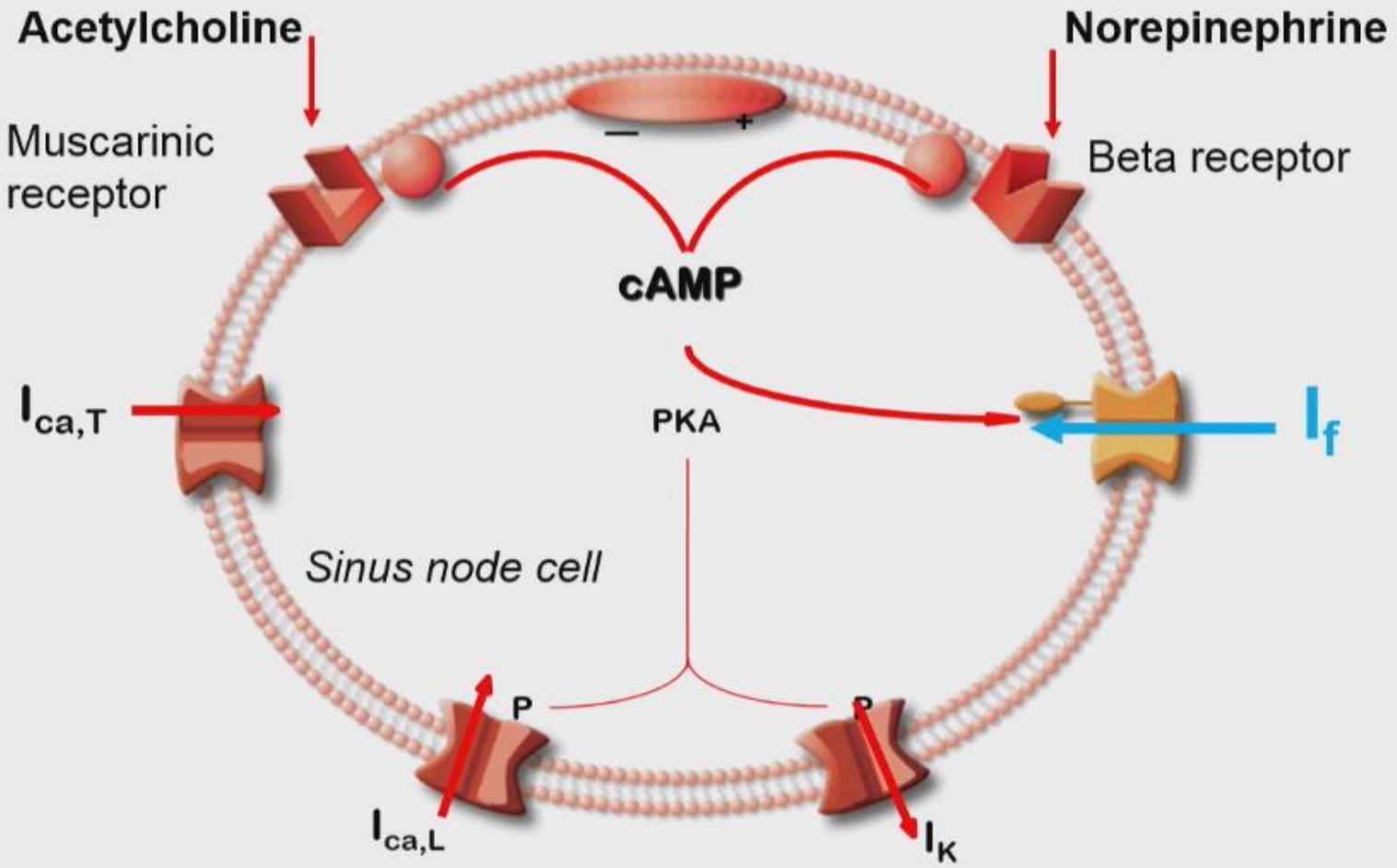
Heart Rate as a Predictor of Death and/or HF Hospitalizations in Chronic HF (SHIFT placebo group)



Increase in risk by 2.9% per 1 bpm ⇧; 15.6% per 5 bpm ⇧

Bohm M, et al. *Lancet*. 2010;376(9744):886-894.

Heart Rate Control



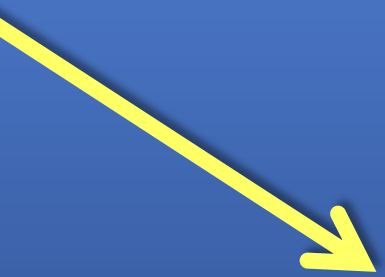
I_f, a hyperpolarization-activated pacemaker current;
Slows diastolic depolarization in the SA node

Verkerk AO et al. *Euro Heart J.* 2007;28:2472-2478.

Ivabradine

Ivabradine acts on the If inward current in the SA node, resulting in reduction of heart rate. It reduces hospital admission and mortality rates in patients with heart failure due to moderate or severe left ventricular systolic impairment. In trials, its effects were most marked in patients with a relatively high heart rate (over 77/min), so ivabradine is best suited to patients who cannot take β-blockers or in whom the heart rate remains high despite β-blockade. It is ineffective in patients in atrial fibrillation.

BNP, ANP, CNP
Bradykinin
Adrenomedullin



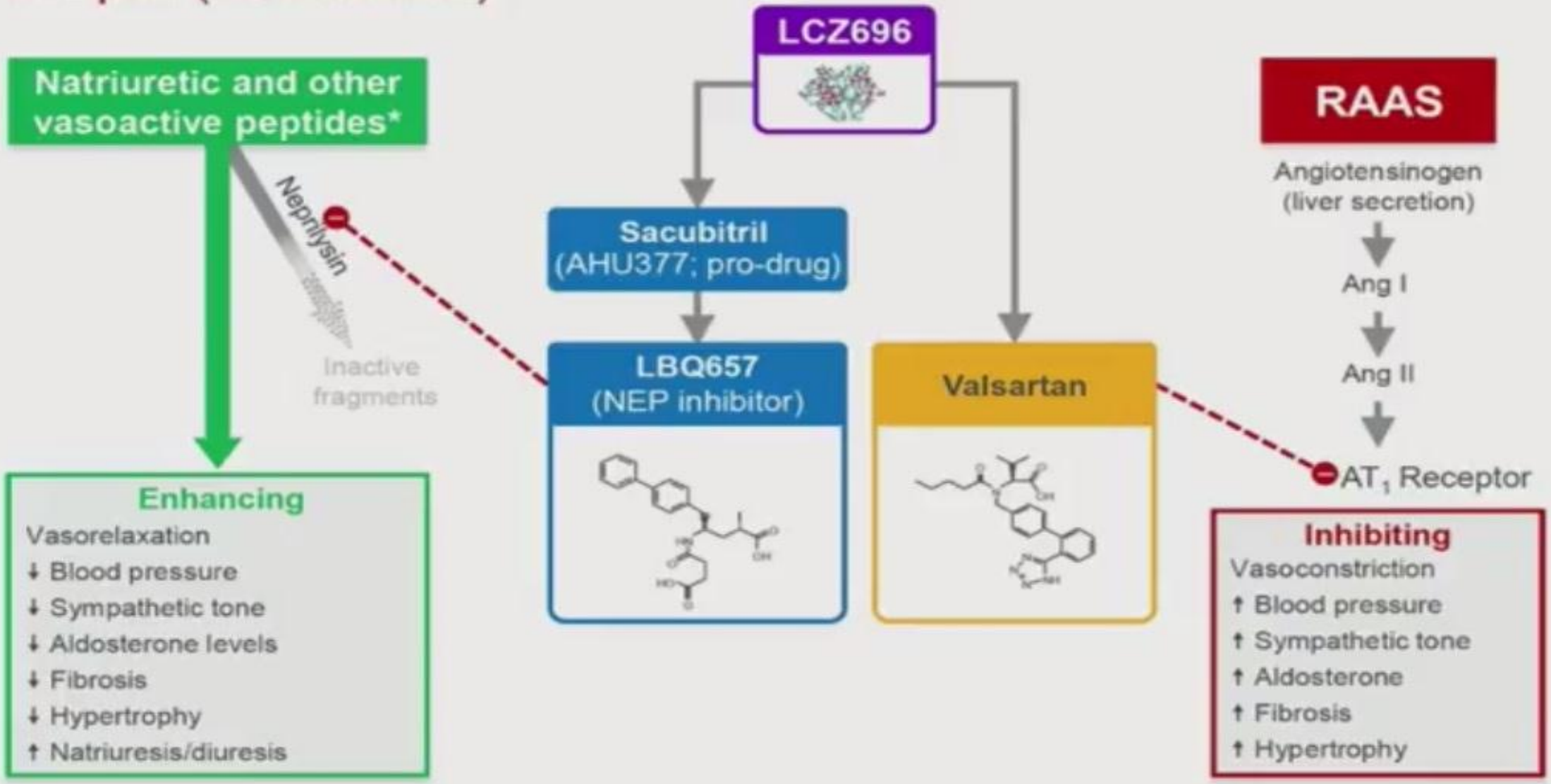
Favorable effects

- Vasodilation
- Decrease SNS
- Natriuresis / diuresis

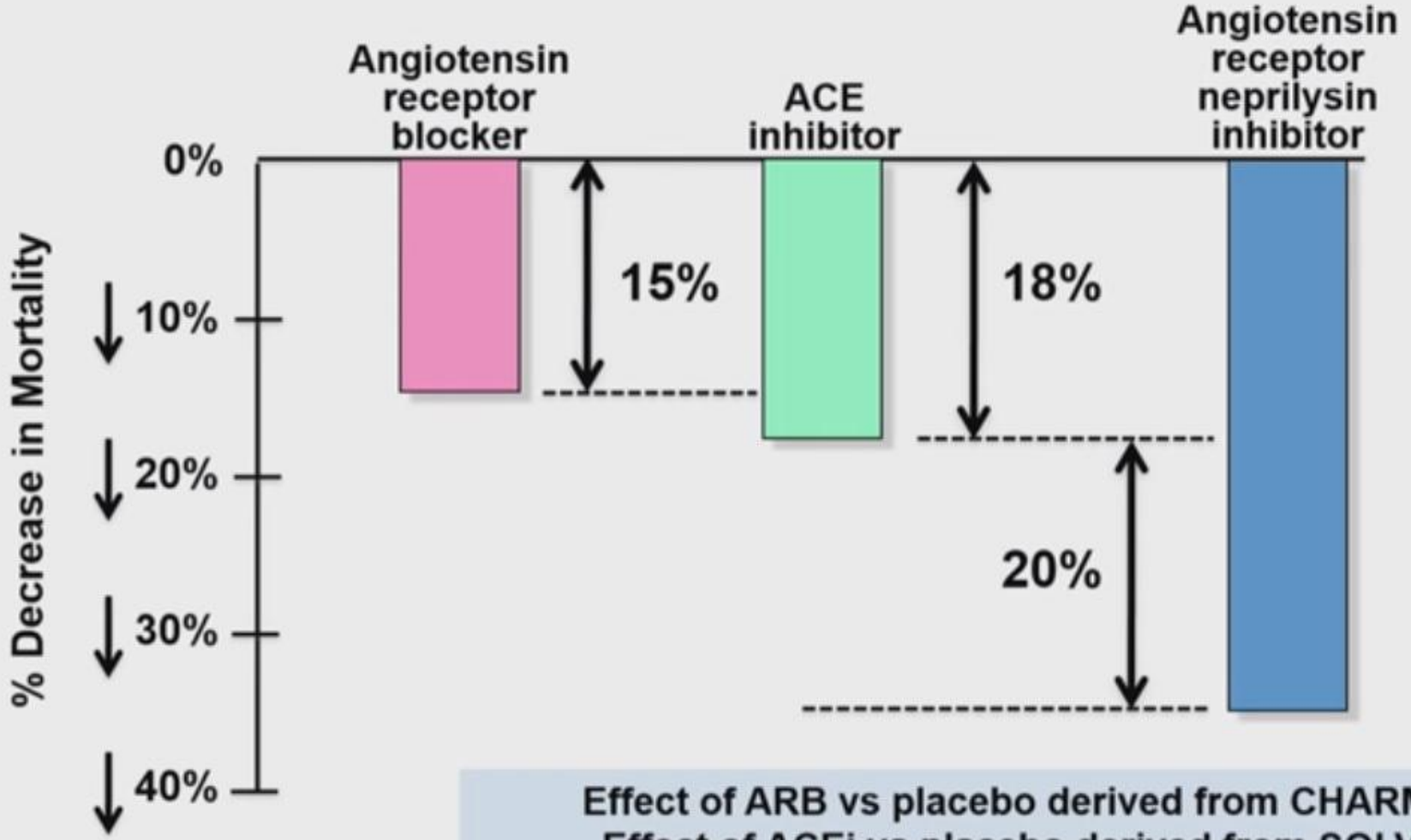
Neprilysin
(neutral endopeptidase)

Inactive fragments

LCZ696 simultaneously inhibits NEP (via LBQ657) and blocks the AT_1 receptor (via valsartan)



ARNI Doubles Effect on Cardiovascular Death of Current Inhibitors of the RAS



Effect of ARB vs placebo derived from CHARM-Alternative trial
Effect of ACEi vs placebo derived from SOLVD-Treatment trial
Effect of ARNI vs ACE inhibitor derived from PARADIGM-HF trial

Digoxin

Digoxin can be used to provide rate control in patients with heart failure and atrial fibrillation. In patients with severe heart failure (NYHA class III–IV, digoxin reduces the likelihood of hospitalisation for heart failure, although it has no effect on long-term survival.

Amiodarone

This is a potent anti-arrhythmic drug that has little negative inotropic effect and may be valuable in patients with poor left ventricular function. It is only effective in the treatment of symptomatic arrhythmias, and should not be used as a preventative agent in asymptomatic patients.

Implantable cardiac defibrillators and resynchronisation therapy

Patients with symptomatic ventricular arrhythmias and heart failure have a very poor prognosis. Irrespective of their response to anti-arrhythmic drug therapy, all should be considered for implantation of a cardiac defibrillator because it improves survival.

. In patients with marked intraventricular conduction delay, prolonged depolarisation may lead to uncoordinated left ventricular contraction.

When this is associated with severe symptomatic heart failure, cardiac resynchronization therapy should be considered. Here, both the LV and RV are paced simultaneously to generate a more coordinated left ventricular contraction and improve cardiac output.

This is associated with improved symptoms and survival.

Coronary revascularisation

Coronary artery bypass surgery or percutaneous coronary intervention may improve function in areas of the myocardium that are 'hibernating' because of inadequate blood supply, and can be used to treat carefully selected patients with heart failure and coronary artery disease. If necessary, 'hibernating' myocardium can be identified by stress echocardiography and specialized nuclear or MR imaging.

Heart transplantation

Cardiac transplantation is an established and successful treatment for patients with intractable heart failure. Coronary artery disease and dilated cardiomyopathy are the most common indications.

The introduction of ciclosporin for immunosuppression has improved survival, which is around 80% at 1 year. The use of transplantation is limited by the efficacy of modern drug and device therapies, as well as the availability of donor hearts, so it is generally reserved for young patients with severe symptoms despite optimal therapy.

Conventional heart transplantation is contraindicated in patients with pulmonary vascular disease due to long-standing left heart failure, complex congenital heart disease (e.g. Eisenmenger's syndrome) or primary pulmonary hypertension because the RV of the donor heart may fail in the face of high pulmonary vascular resistance. However, heart–lung transplantation can be successful in patients with Eisenmenger's syndrome. Lung transplantation has been used for primary pulmonary hypertension.

Although cardiac transplantation usually produces a dramatic improvement in the recipient's quality of life, serious complications may occur:

• *Rejection*. In spite of routine therapy with ciclosporin A, azathioprine and corticosteroids, episodes of rejection are common and may present with heart failure, arrhythmias or subtle ECG changes; cardiac biopsy is often used to confirm the diagnosis before starting treatment with high-dose corticosteroids.

• *Accelerated atherosclerosis*. Recurrent heart failure is often due to progressive atherosclerosis in the coronary arteries of the donor heart. This is not confined to patients who underwent transplantation for coronary artery disease and is probably a manifestation of chronic rejection. Angina is rare because the heart has been denervated.

• *Infection*. Opportunistic infection with organisms such as cytomegalovirus or *Aspergillus* remains amajor cause of death in transplant recipients.

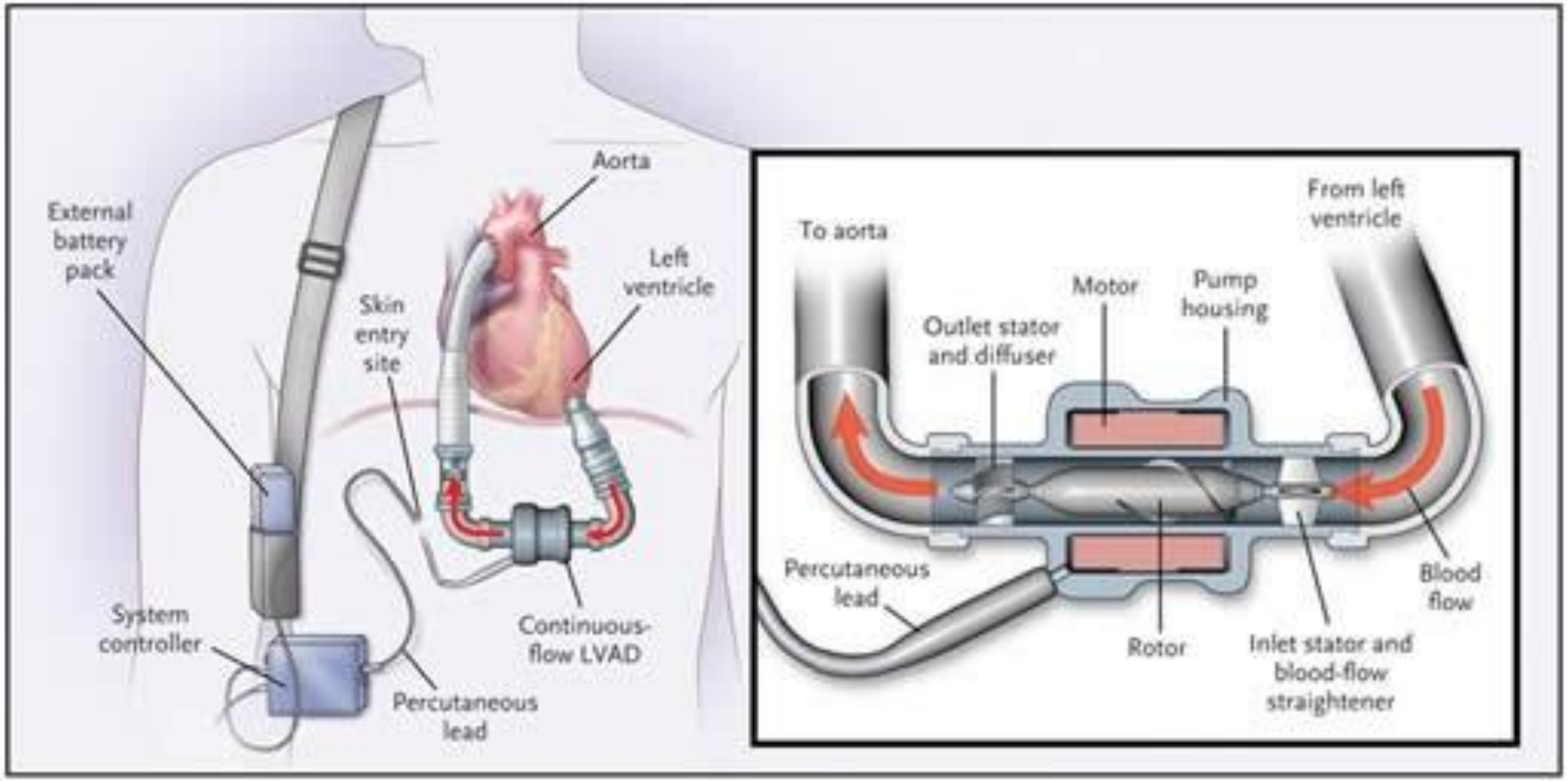
Ventricular assist devices

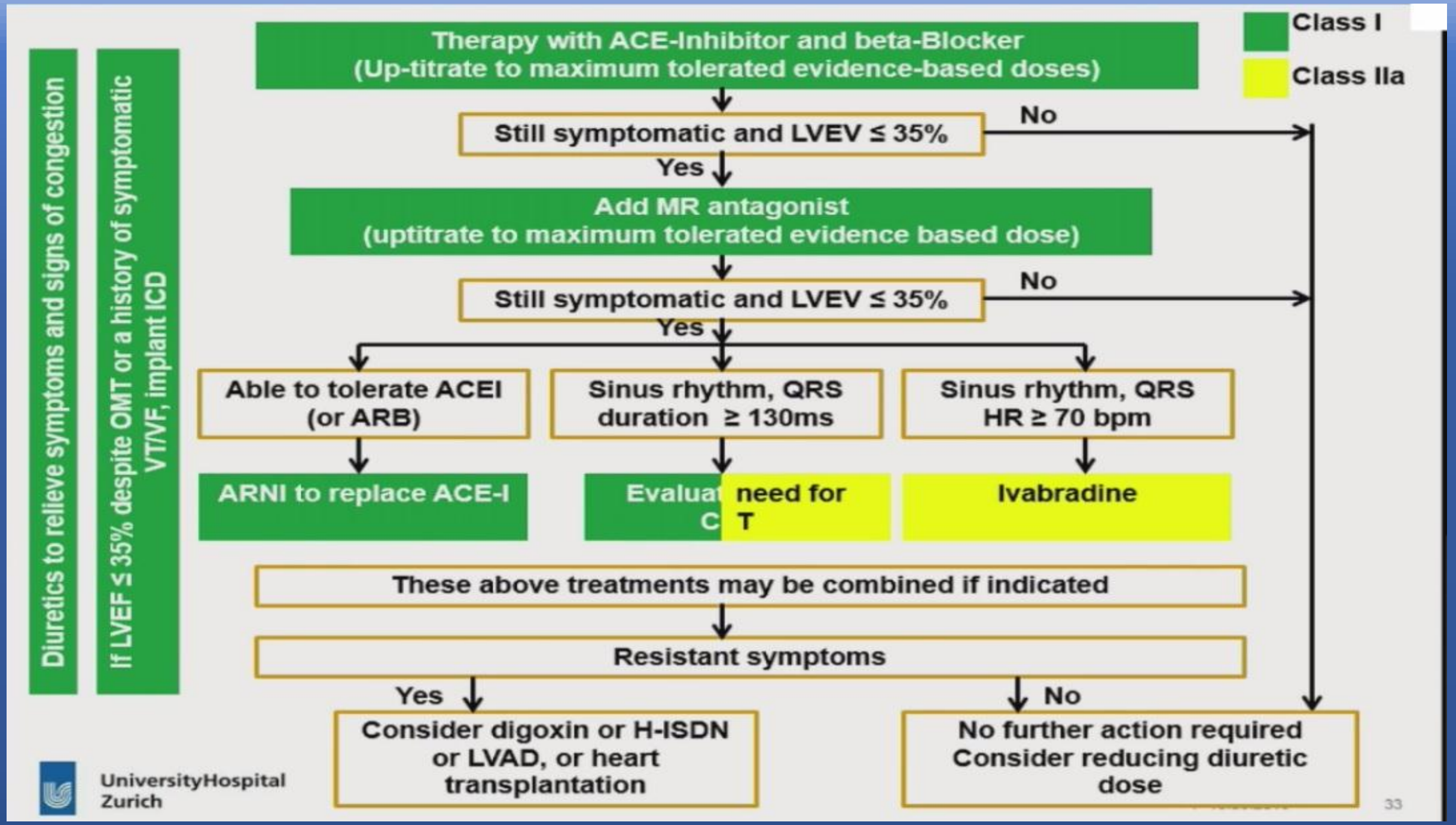
Because of the limited supply of donor organs, ventricular assist devices (VADs) have been employed as:

- a bridge to cardiac transplantation
- potential long-term therapy
- short-term restoration therapy following a potentially reversible insult, e.g. viral myocarditis.

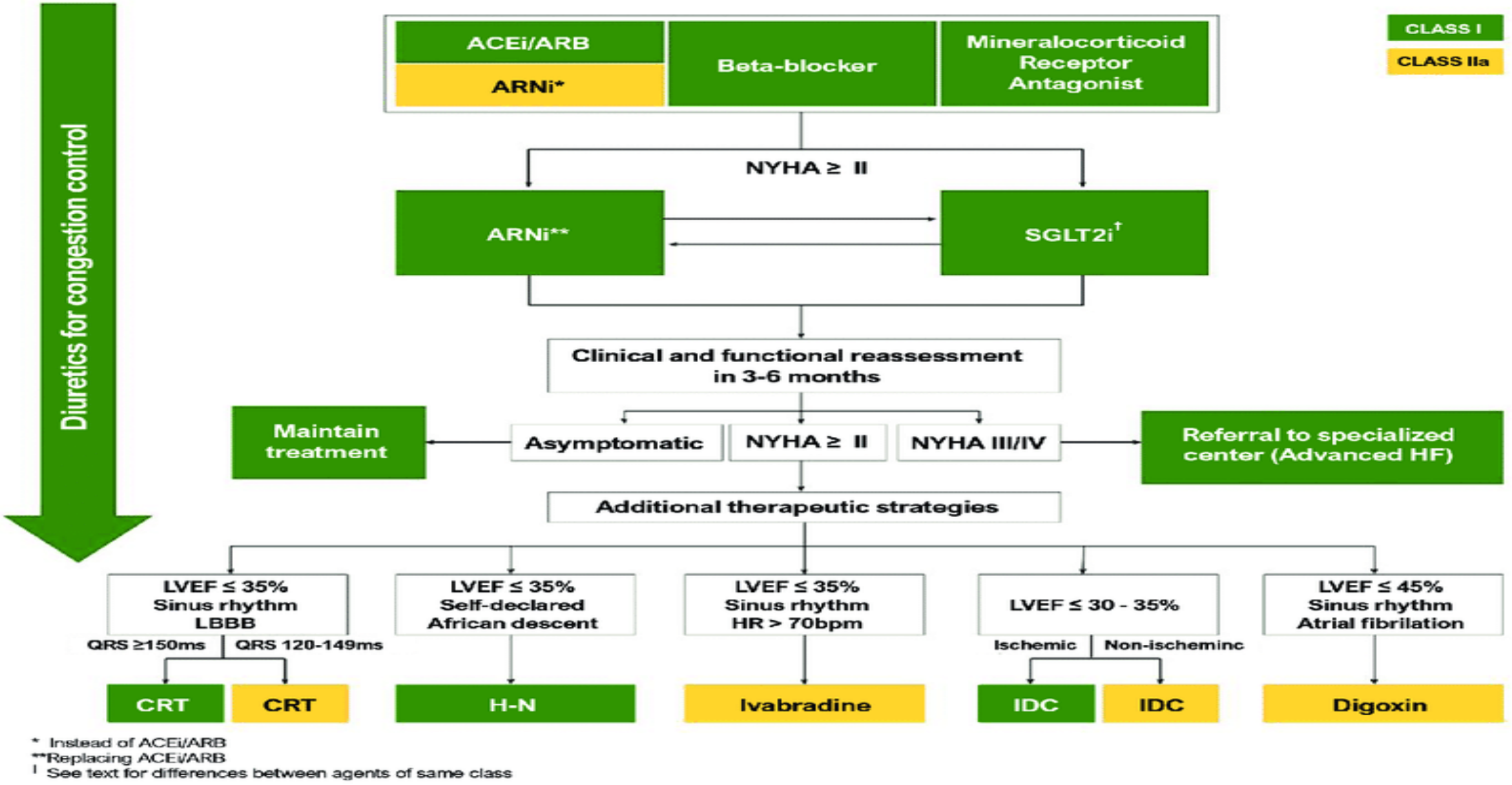
VADs assist cardiac output by using a roller, centrifugal or pulsatile pump that, in some cases, is implantable and portable. They withdraw blood through cannulae inserted in the atria or ventricular apex and pump it into the pulmonary artery or aorta. They are designed not only to unload the ventricles but also to provide support to the pulmonary and systemic circulations. Their more widespread application is limited by high complication rates (haemorrhage, systemic embolism, infection, neurological and renal sequelae), although some improvements in survival and quality of life have been demonstrated in patients with severe heart failure.

- In refrctory cases – LVAD
- Heart transplatation




Class I
Class IIa
Therapy with ACE-Inhibitor and beta-Blocker
(Up-titrate to maximum tolerated evidence-based doses)
Still symptomatic and LVEV ≤ 35%
No
Yes
Add MR antagonist
(uptitrate to maximum tolerated evidence based dose)
Still symptomatic and LVEV ≤ 35%
No
Yes
Able to tolerate ACEI
(or ARB)
Sinus rhythm, QRS
duration ≥ 130ms
Sinus rhythm, QRS
HR ≥ 70 bpm
ARNI to replace ACE-I
Evaluat need for
C T
Ivabradine
These above treatments may be combined if indicated
Resistant symptoms
Yes
No
Consider digoxin or H-ISDN
or LVAD, or heart
transplantation
No further action required
Consider reducing diuretic
dose
Diuretics to relieve symptoms and signs of congestion
If LVEF ≤ 35% despite OMT or a history of symptomatic VT/VF, implant ICD
UniversityHospital
Zurich
33

Heart Failure with Reduced Ejection Fraction (NYHA II-IV/Stage C)



* Instead of ACEi/ARB
**Replacing ACEi/ARB
† See text for differences between agents of same class

Drugs *not recommended*

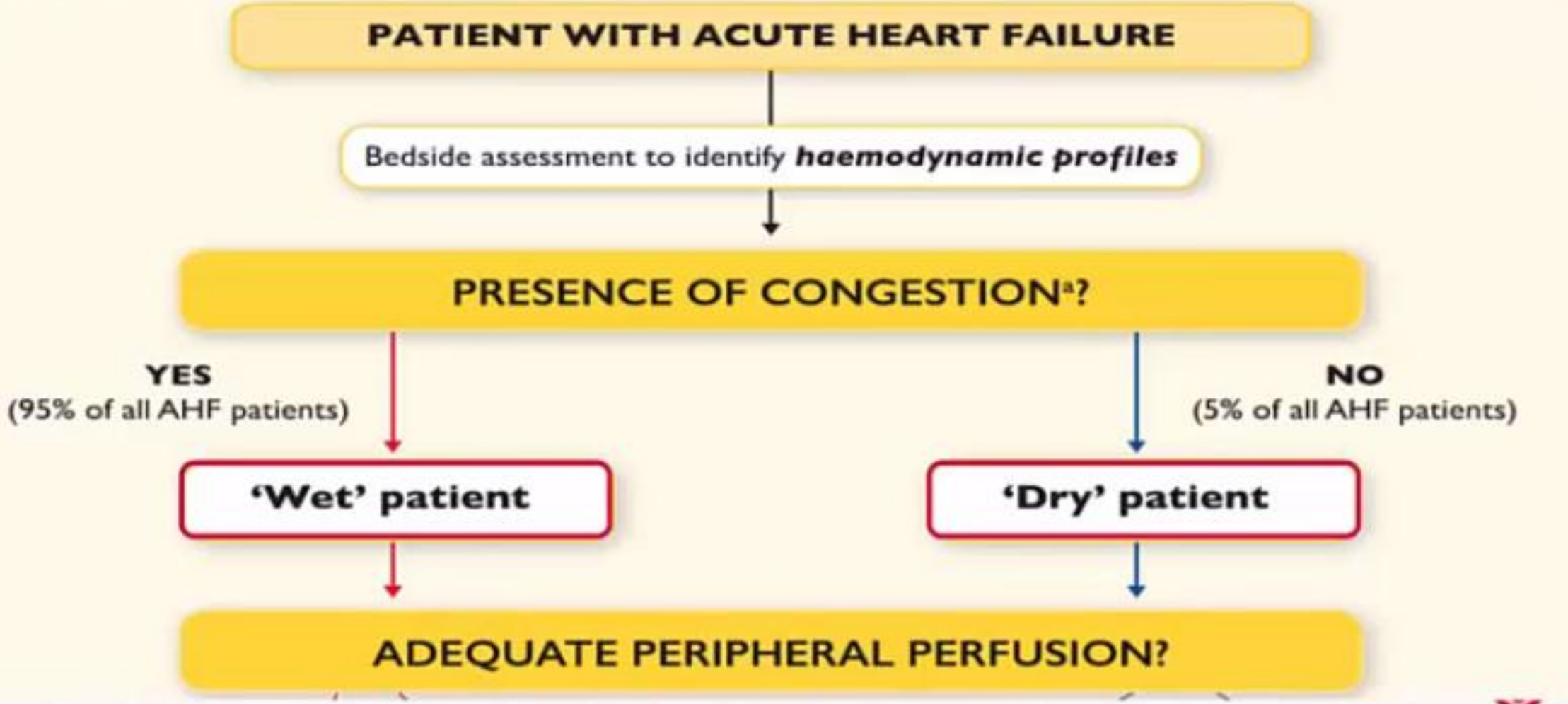
Recommendations		
No Thiazolidinediones (glitazones)	III	A
No NSAID's or COX-2 inhibitors	III	B
No Diltilazem or Verapamil	III	C
No addition of an ARB (or renin inhibitor) to the combination of ACEI or MRA	III	C

Heart Failure Guidelines EHJ / EJHF 2016

CCU/ICU ADMISSION?

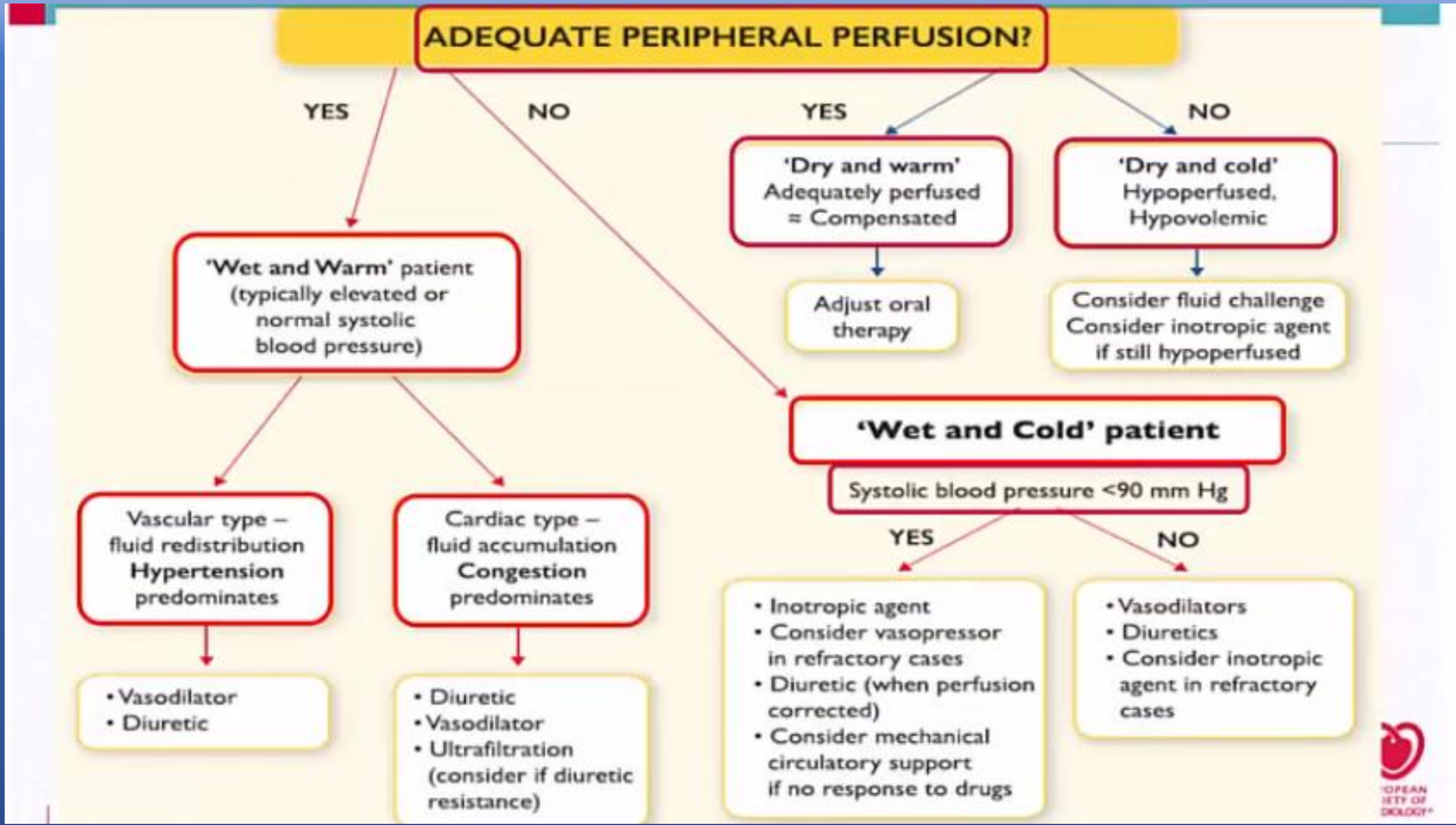
- For high-risk patients (i.e. with persistent, significant dyspnoea, haemodynamic instability, recurrent arrhythmias, AHF and associated ACS).
- **The criteria for ICU/CCU admission include any of the following:**
- – need for intubation (or already intubated)
- – signs/symptoms of hypoperfusion
- – oxygen saturation (SpO2) <90% (despite supplemental oxygen)
- – use of accessory muscles for breathing, respiratory rate .25/min
- – heart rate <40 or >130 bpm, SBP <90 mmHg

Management of patients with acute heart failure based on clinical profile during an early phase

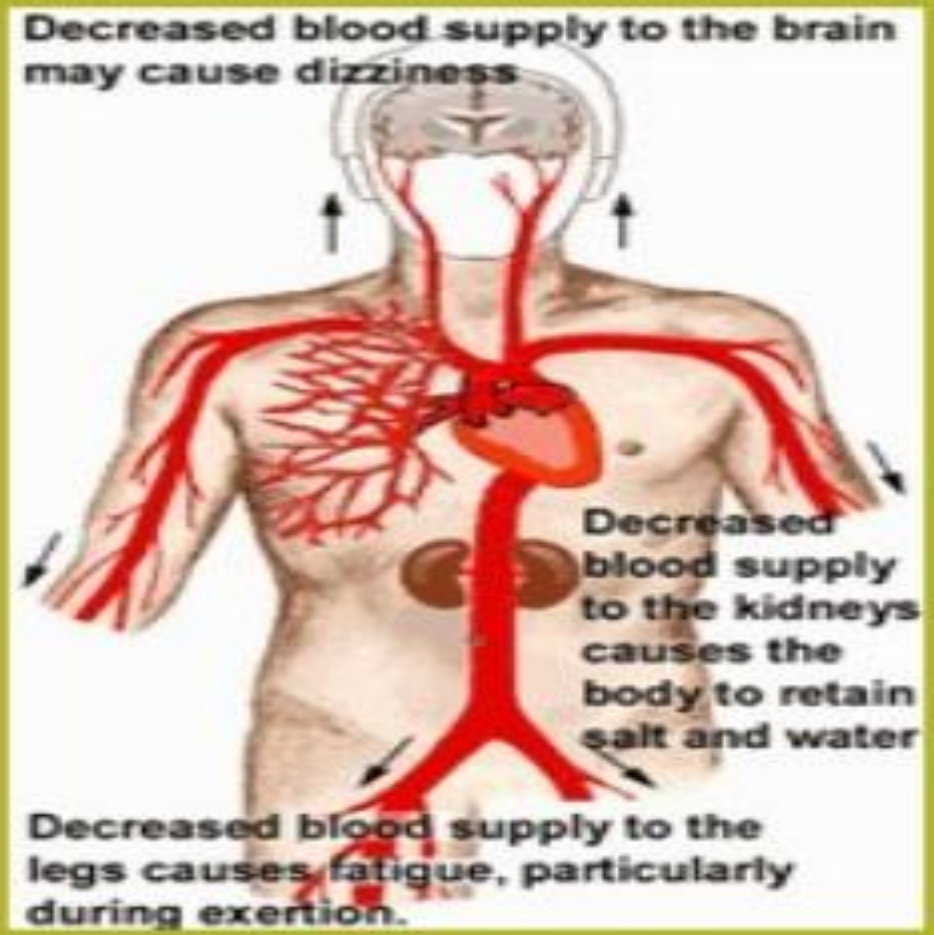


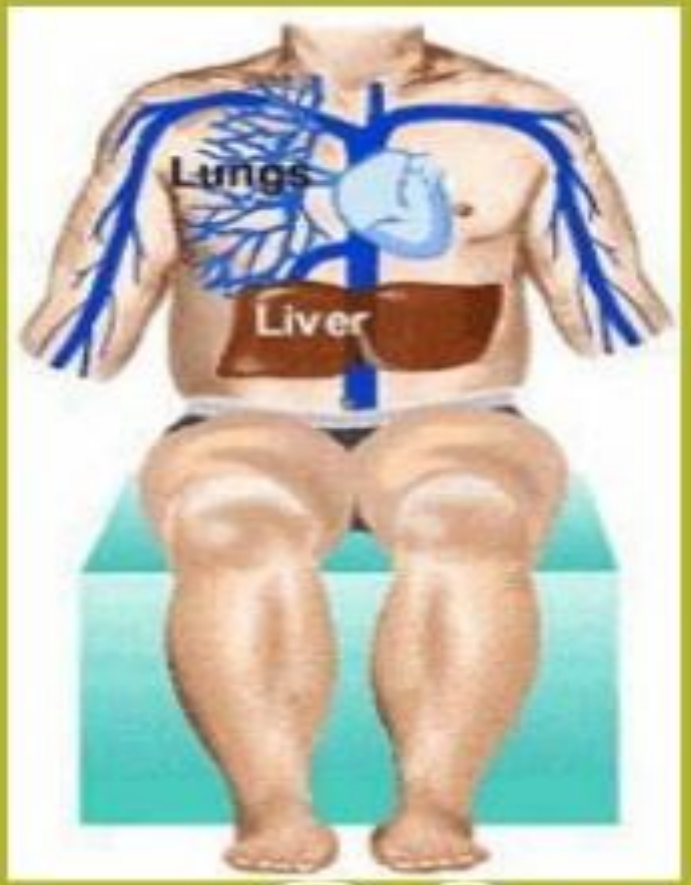
www.escardio.org/guidelines

EUROPEAN SOCIETY OF CARDIOLOGY


ADEQUATE PERIPHERAL PERFUSION?
YES
NO
'Wet and Warm' patient (typically elevated or normal systolic blood pressure)
Vascular type – fluid redistribution Hypertension predominates
• Vasodilator
• Diuretic
Cardiac type – fluid accumulation Congestion predominates
• Diuretic
• Vasodilator
• Ultrafiltration (consider if diuretic resistance)
YES
NO
'Dry and warm' Adequately perfused ≈ Compensated
Adjust oral therapy
'Dry and cold' Hypoperfused, Hypovolemic
Consider fluid challenge
Consider inotropic agent if still hypoperfused
'Wet and Cold' patient
Systolic blood pressure <90 mm Hg
YES
NO
• Inotropic agent
• Consider vasopressor in refractory cases
• Diuretic (when perfusion corrected)
• Consider mechanical circulatory support if no response to drugs
• Vasodilators
• Diuretics
• Consider inotropic agent in refractory cases

Heart Failure





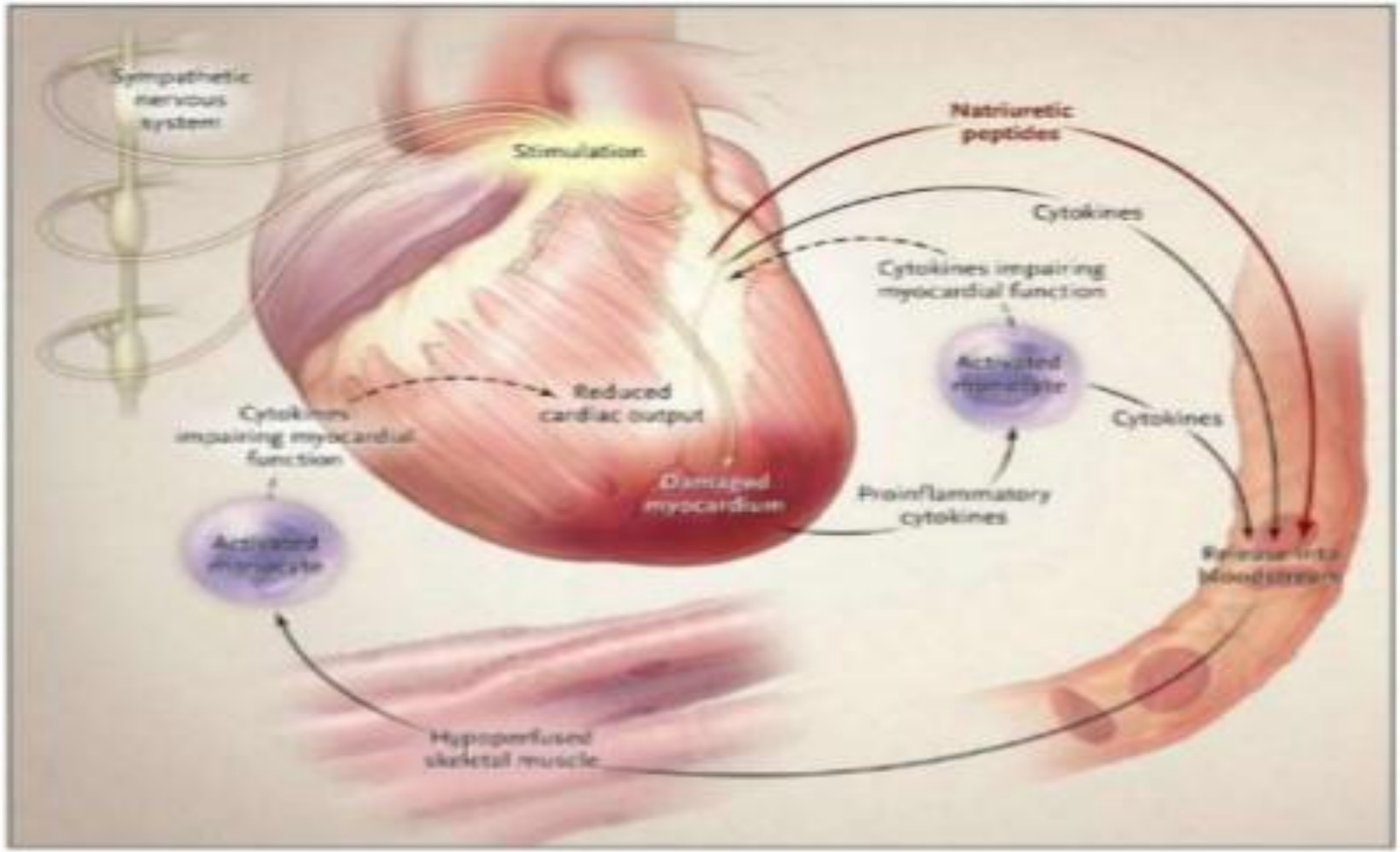
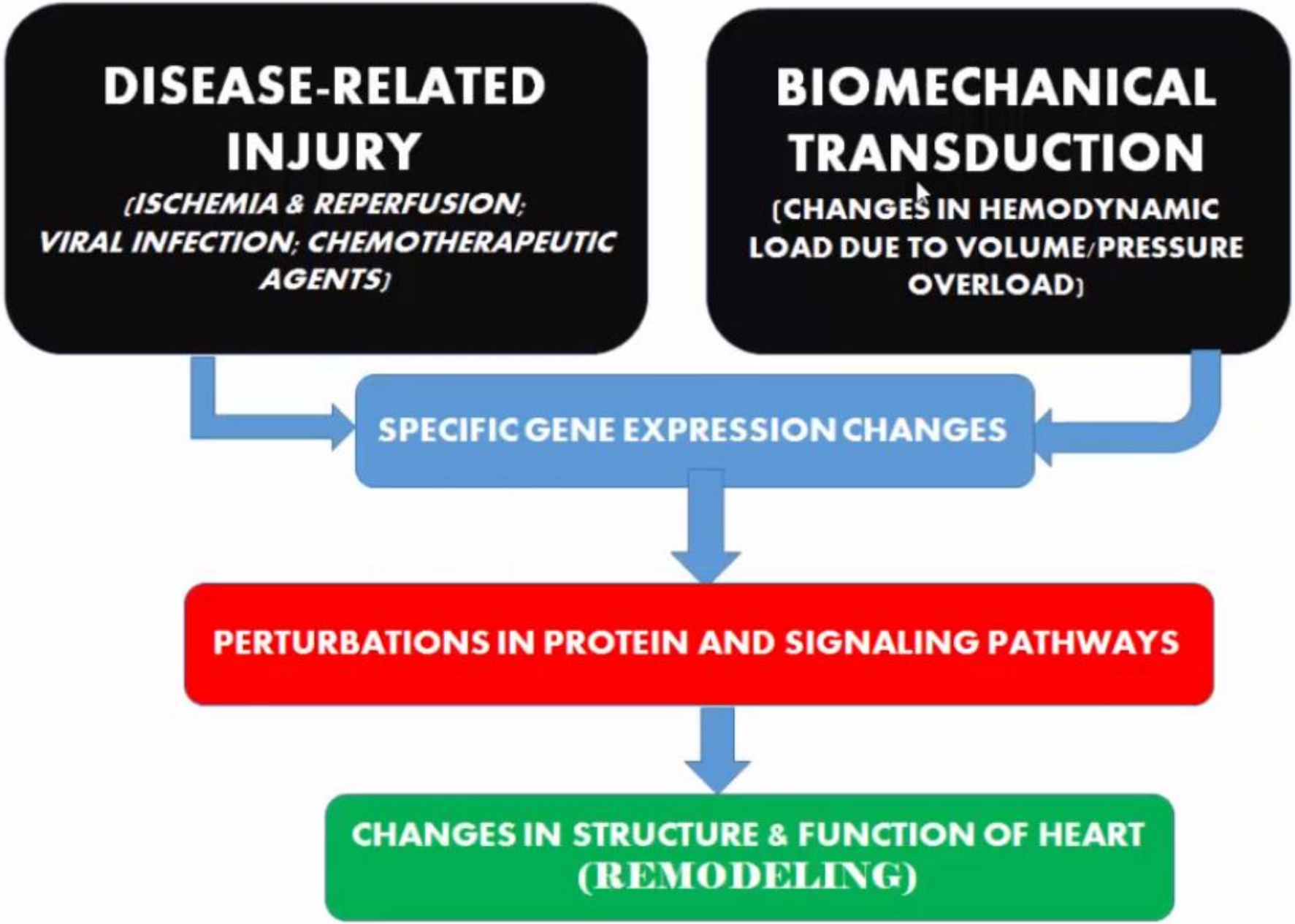


Figure 1. The Cytokine Hypothesis of Heart Failure.

According to the cytokine hypothesis of heart failure, proinflammatory cytokines (tumor necrosis factor α, interleukin-1, interleukin-6, and interleukin-18) are produced by the damaged myocardium; this production is enhanced by stimulation of the sympathetic nervous system. Injured myocardium, as well as skeletal muscle that is hypoperfused because of reduced cardiac output, activates monocytes to produce the same cytokines, which act on and further impair myocardial function (dashed lines). Cytokines from these several sources are also released into the bloodstream. The stressed myocardium releases natriuretic peptides, denoted in red; their release improves the circulation. Adapted from Anker and von Haehling3 and Seta et al.11


DISEASE-RELATED INJURY
(ISCHEMIA & REPERFUSION; VIRAL INFECTION; CHEMOTHERAPEUTIC AGENTS)
BIOMECHANICAL TRANSDUCTION
(CHANGES IN HEMODYNAMIC LOAD DUE TO VOLUME/PRESSURE OVERLOAD)
SPECIFIC GENE EXPRESSION CHANGES
PERTURBATIONS IN PROTEIN AND SIGNALING PATHWAYS
CHANGES IN STRUCTURE & FUNCTION OF HEART
(REMODELING)

General Measures

Lifestyle Modifications:

- Weight reduction
- Discontinue smoking
- Avoid alcohol and other **cardiotoxic substances**
- Exercise

Medical Considerations:

- Treat HTN, hyperlipidemia, diabetes, arrhythmias, hyperthyroidism , infections , anemia , endocarditis.
- Surgical Repair of cardiac defects
- Coronary revascularization
- Anticoagulation
- Sodium restriction
- Daily weights
- Close outpatient monitoring

Pharmacologic Management

Diuretics

- Used to relieve fluid retention
- Improve exercise tolerance
- Facilitate the use of other drugs indicated for heart failure
- Patients can be taught to adjust their diuretic dose based on changes in body weight
- Electrolyte depletion a frequent complication
- Should never be used alone to treat heart failure
- Higher doses of diuretics are associated with increased mortality

Pharmacologic Management

ACE Inhibitors

- Blocks the conversion of angiotensin I to angiotensin II; prevents functional deterioration
- Recommended for all heart failure patients
- Relieves symptoms and improves exercise tolerance
- Reduces risk of death and decreases disease progression
- Benefits may not be apparent for 1-2 months after initiation

Pharmacologic Management

Beta-Blockers

- Cardioprotective effects due to blockade of excessive SNS stimulation
- In the short-term, beta blocker decreases myocardial contractility; increase in EF after 1-3 months of use
- Long-term, placebo-controlled trials have shown symptomatic improvement in patients treated with certain beta-blockers[1]
- When combined with conventional HF therapy, beta-blockers reduce the combined risk of morbidity and mortality, or disease progression

1 Hunt, SA, et al ACC/AHA Guidelines for the Evaluation and Management of Chronic Heart Failure in the Adult, 2001 p. 20.

Pharmacologic Management

Aldosterone Antagonists

- Generally well-tolerated
- Shown to reduce heart failure-related morbidity and mortality
- Generally reserved for patients with NYHA Class III-IV HF
- Side effects include hyperkalemia and gynecomastia. Potassium and creatinine levels should be closely monitored

Pharmacologic Management

Angiotensin Receptor Blockers (ARBs)

- Block AT_1 receptors, which bind circulating angiotensin II
- Examples: valsartan, candesartan, losartan
- Should not be considered equivalent or superior to ACE inhibitors
- In clinical practice, ARBs should be used to treat patients who are ACE intolerant due to intractable cough or who develop angioedema

Pharmacologic Management

Digoxin

- Enhances inotropy of cardiac muscle
- Reduces activation of SNS and RAAS
- Controlled trials have shown long-term digoxin therapy:
  - Reduces symptoms
  - Increases exercise tolerance
  - Improves hemodynamics
  - Decreases risk of HF progression
  - Reduces hospitalization rates for decompensated HF
  - Does not improve survival

NITRATES
CLINICAL USES

- Pulmonary congestion
- Orthopnea and paroxysmal nocturnal dyspnea
- CHF with myocardial ischemia
- In acute CHF and pulmonary edema: NTG s.l. or i.v.

CALCIUM ANTAGONISTS
POSSIBLE UTILITY

Diltiazem contraindicated

Verapamil and Nifedipine not recommended

Vasoselective (amlodipine, nisoldipine), may be useful in ischemia + CHF

Amlodipine may be useful in nonischemic CHF

THANK YOU